STATE OF MINNESOTA DISTRICT COURT

COUNTY OF RAMSEY SECOND JUDICIAL DISTRICT

- -

The State of Minnesota,
by Hubert H. Humphrey, III,
its attorney general,
and
Blue Cross and Blue Shield
of Minnesota,

Plaintiffs,

vs. File No. C1-94-8565

Philip Morris Incorporated, R.J.
Reynolds Tobacco Company, Brown
& Williamson Tobacco Corporation,
B.A.T. Industries P.L.C., Lorillard
Tobacco Company, The American
Tobacco Company, Liggett Group, Inc.,
The Council for Tobacco Research-U.S.A.,
Inc., and The Tobacco Institute, Inc.,

Defendants.

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DEPOSITION OF DAVID G. BENDITT, M.D.

Volume I, Pages 1 - 200

(The following is the Deposition of DAVID G. BENDITT, M.D., taken pursuant to Notice of Taking Deposition, at the offices of Dorsey & Whitney, Attorneys at Law, 220 South Sixth Street, Minneapolis, Minnesota, on September 15, 1997, commencing at approximately 8:33 o'clock a.m.)

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E X A M I N A T I O N I N D E X

E X H I B I T I N D E X

		AHA, 6 pgs.	
	3803	Pamphlet, "Smoking and Heart	35
		Disease," 12 pgs.	
	3804	"Cigarette Smoking and	35
		Cardiovascular Diseases," 1 pg.	
	3805	"Cigarette Advertising," AHA,	35
		1 pg.	
	3806	Defendant's Expert Report of:	79
		David G. Benditt, MD, 7/1/97	

P R O C E E D I N G S

(Plaintiffs' Deposition Exhibit 3800 was marked for identification.)

(Witness sworn.)

DAVID G. BENDITT, M.D.

called as a witness, being first duly sworn, was examined and testified as follows:

ADVERSE EXAMINATION

BY MS. FLYNN PETERSON:

Q. Good morning, Dr. Benditt.

A. Good morning.

Q. I introduced myself a few minutes ago. I'm Kathleen Flynn Peterson. Have you had your deposition taken before, sir?

A. Yes, I have.

Q. If at any time this morning you do not understand or don't hear a question that I ask, would you please let me know and I will gladly repeat or rephrase the question.

A. Will do.

Q. You understand the testimony you are giving here this morning has the same force and effect as if you were testifying in a courtroom?

A. I do.

Q. You understand that you are under oath?

A. Yes.
Q. And that oath has the same force and effect as one that would be given in a courtroom before testifying?
A. Yes.
Q. Dr. Benditt, as we begin this morning, I wanted to review with you some background information regarding your education and experience and practice. You are a cardiologist, sir?
A. That's correct.
Q. I understand from a review of your curriculum vitae you are at practice at the University of Minnesota?
A. That's correct.
Q. As we began this morning, I had marked as a deposition exhibit the copy of your curriculum vitae that has now been marked as Plaintiffs' Exhibit 3800 and dated today's date of 9/15/97. Sir, is that the most recent curriculum vitae?
A. Yes, this is correct up to May 1997.
Q. And so as of today, in September, that would be the most recent curriculum vitae that you have?
A. That's correct.
Q. Is it true, Dr. Benditt, your specialty within cardiology is electrophysiology?

A. That's correct.
Q. As I have reviewed the bibliography of your articles that appears in your curriculum vitae, it appears that every one of your published writings has to do with electrophysiology or arrhythmias or disarrhythmias; would that be correct?
A. That's correct.
Q. Sir, have you ever done any research on the effect of tobacco smoking or cigarette smoking and cardiovascular disease?
A. No.
Q. Have you ever published any articles relating to the relationship between tobacco use or cigarette smoking and cardiovascular disease?
A. No.
Q. Have you ever done any research regarding the relationship of tobacco smoking to tobacco use and atherosclerosis?
A. No.
Q. Would that be true also with cerebral vascular diseases?
A. That's correct.
Q. Dr. Benditt, you are not relying on any of your personal research or publications in the opinions that you have expressed in this litigation, are you?

A. That's not correct.
Q. Okay. In what way is it not correct?
A. Well my research directly bears on the occurrence of death in patients and in our patient population that strongly relates to cardiovascular disease and that's directly related to our clinical research and heart-rhythm disturbances and related conditions.
Q. And in that research, sir, can you explain for me, then, what you are relying on as it relates to your opinions in this litigation?
A. The experience that we have in taking care of patients with multiple disease conditions of which cardiovascular disorders are a manifestation and the consequences of those cardiovascular disorders.
Q. Can you tell me specifically in your own research regarding death related to cardiovascular disease what you have learned relative to the patients who have smoked, smoking history, cigarette smoking history or tobacco use?
A. Well I think the most important item is that there is a number of factors in every one of those patients which relate to why they manifest the disease condition, and when we take histories and write about those patients, both in their medical

history and in the scientific literature, it's commonly recognized that these patients have many factors that go into their disease condition and manifestation of those diseases.

Q. And what has been your experience, sir, with respect to the specific relation of cigarette smoking and tobacco use to what you found?

A. It's one of the factors that plays a role in cardiovascular diseases.

Q. And is that supported by your research?

A. It's supported by my research and -- as it relates to clinical experience and clinical research, yes.

Q. Is there any of your specific articles or research studies that you are relying on in expressing those opinions here today?

A. There is at least one in there that relates to the occurrence of sudden death in a patient population. There are probably several in there that relate to sudden death, in the CV that is.

Q. Referring again to Exhibit 3800, would you please tell me specifically, when you said one of the articles related to sudden death, which one that would be, sir?

A. Take me a moment to go through this.

Q. That's fine.
A. I'm actually going to point out several articles that relate to sudden death and in whom patients had multiple factors related to the occurrence of sudden death, or lethal ventricle arrhythmias is another way we look at it.
Q. Would cigarette smoking be one of those factors?
A. One of those factors. I'll give you the reference numbers. Would that be fine?
Q. That would be fine, as reflected on Exhibit 3800.
A. Correct. Number 7, number 14. This is a -- Number 14 is a basic science article. It doesn't reflect clinical; it reflects basic laboratory science. And I mention it only so that we have it down there if you want to come back to it.
Number 20, number 25, number 28, number 35, 36, 38. Thirty-eight doesn't deal directly with smoking but deals with other factors that cause manifestations that are very similar, as does number 40. Number 54, again an experimental study; number 82; and number 86, again an experimental study that links indirectly to the occurrence of arrhythmias with -- with other cause -- of other causes. Number 115, that one is somewhat indirect but worth noting;

number 121 falls in that category, too, and number 123. And there may be some others in there that are indirect but perhaps less direct than the ones I've mentioned.

Q. In each of the references that you have just told us about, it has been your experience in finding cigarette smoking played a role in development of arrhythmias?

A. No, each of the references that talk about cigarette smoking may have played a role. There are also a number of references in there that point out that other disease processes also, either exclusively or in conjunction with cigarette smoking or other risk factors, have played a role in the development of cardiovascular disease in various manifestations, and as in our particular interest, the manifestation of heart-rhythm disturbances or sudden death as part of that picture.

Q. Dr. Benditt, it is not your opinion that cigarette smoking does not play a role in the development of coronary vascular disease, is it?

A. You had too many negatives in there for me. Can you do it in a positive fashion?

Q. You would agree that cigarette smoking does play a role in the development of coronary vascular

disease?

A. If by "role" you mean is it a risk factor that's associated with cardiovascular disease, yes.

Q. In reviewing your curriculum vitae, I note that you have worked as an investigator for the American Heart Association.

A. That's correct.

Q. Tell me what that role is.

A. I have worked as an investigator supported by the American Heart Association as opposed to working for the American Heart Association. That's an important distinction, I think. I've had research grants supported by both the Minnesota affiliate of the American Heart Association and by the national organization, and that at one time between 1981 and 1985, something in that range, I was supported by a national grant. All of the research I think can be generalized into the category of the evaluation of factors that result in heart-rhythm disturbances, particularly lethal or potentially lethal heart-rhythm disturbances.

Q. In that investigation, have you ever investigated the role of cigarette smoking or tobacco use?

A. Not directly in those experimental studies. The

grants related to experimental studies in animals, and predominantly dogs, and none of those studies were directly related to, you know, inhalation experiments, you know, that kind of thing in canines.

Q. What is the American Heart Association?

A. The American Heart Association is an organization which I will give you my view of, may not be accurate. It's a national organization whose mission is to foster education and research and publish information related to heart disease and try to foster, through education processes, changes in public habits that might reduce the impact of heart disease, including stroke. I should put that in there. It's really cardiovascular disease because it includes stroke and hypertension, to reduce the impact of those conditions on the public health, adverse impact.

Q. And that is a mission you have supported in your professional work, isn't it, sir?

A. That is correct.

Q. You have actually served in positions with the American Heart Association?

A. Yes. I served in a number of positions. I directed, at one point, the research activities of the American Heart Minnesota affiliate and I was

president of the American Heart Minnesota affiliate as well. I can't remember the exact years but not too long.

Q. Early '90s as I recall from your curriculum vitae.

A. Uh-huh.

Q. What is the responsibilities of the president of the Minnesota affiliate?

A. Primarily the Minnesota affiliate president is a physician slash scientist whose job is to oversee both the scientific aspects of the affiliate which is supporting research, and the support of research also entails the peer review of -- of research applications. The president also is -- supports, in conjunction with the chairman of the board, the public relations/public education aspects of the organization which, as I alluded to earlier, takes the -- the role of trying to modify public attitudes and habits, if you will, to better -- or to reduce the impact of cardiovascular disease in the population.

Q. You said one of the responsibilities was to oversee scientific aspects. Explain for me more specifically what that would entail.

A. The president is sort of the individual who

focuses for their term the organization's resources that relate to the evaluation of research proposals that come in from investigators around -- particularly in Minnesota, and then is responsible for the peer review of those; in other words, the assessment of those and the prioritization of those research applications in terms of funding versus not funding. The president also, in conjunction with the chairman of the board, has responsibility for raising awareness of organizations; that is, the heart association organization, as an organization, their function in the community; in other words, trying to persuade more people in the community to support that organization's activities through either volunteer work or financial donations, because it's through volunteer work that education is done in the community and it's through financial support that the research is supported, as well as financial support goes to supporting education of trainees; in other words, usually physicians or scientists who are taking -- who have taken an interest in that general field of cardiovascular disease.

Q. Is the public education information that is published by the American Heart Association valid information for the public to rely on?

A. It's information that has, to the best of the ability of the organization, the intention to try to inform the public as to what we know or what we think we know about cardiovascular disease and how it may -- how it impacts the public and how the public might reduce their own personal risks of cardiovascular disease. Is every word that comes out scientifically valid? I think not. It's an education function that has to be simplified to be understandable to the average individual since we are not talking to, you know, qualified scientists in the community. So it's valid to the extent that it tries to be honest within the realm of also getting a message across just like everybody tries to get a message across through public relations.

Q. Has it been your experience in your work with the American Heart Association that that message has scientific basis?

A. I think the message has reasonable scientific basis, but I wouldn't say that everything that's stated by the American Heart Association has been proven to be scientifically correct.

Q. Would you say that their publications are more probably true than not true?

MR. BORMAN: I'll object to lack of

foundation.

Go ahead.

A. I'm not quite sure what "more probably" means. If you mean 51 percent versus 49 percent, yes.

Q. This -- The public information or the education information that is actually published in written form by the American Heart Association, is there any process that you are aware of through the heart association where they peer review that information and try to make sure that it has scientific basis?

A. I can't speak for the national organization because I'm not intimately familiar with its system, although I know that it's quite extensive and I'm sure there are ways that information is vetted, if you will. The local organization has limited resources in that regard and largely relies upon the national organization in terms of providing materials, and some of those materials may be modified a little bit to fit the region --

Q. Uh-huh.

A. -- that they are used in, but not substantially.

Q. So what is the process, though? Is there any process from the Minnesota affiliate that information is reviewed by their consultants and scientists and

physicians to determine whether it is valid, scientific-based information?

A. At the time I was working more intimately with the information and I'm not now so I can't speak about the present tense.

Q. Let's talk about that time.

A. The materials provided by the national organization would be at least to some extent reviewed by the board, board of trustees of -- who were representatives both of the scientific medical community as well as citizens and -- of various professions so that the information would at least be looked at in terms of does it make sense to put this out in the public domain as an educational piece --

Q. Uh-huh.

A. -- and not in the sense is every sentence of it scientifically substantiated, you know, crossing every "T" and dotting every "I" and providing references. The organization's function was to try to generalize things in a way that made sense to the public, that might change public habits in a way that the organization feels promotes health, and often times that would be based on information that you couldn't in fact go back and say this is scientifically absolutely true.

One of the -- If I may put in a plug for the organization itself, one of the limitations is that there isn't enough financial resources provided for research in this area, and neither government nor the public domain, and particularly the health organizations which profit in many ways from health care, have taken a significant interest in providing the research dollars to support the activity that's needed to provide that scientific research. So we are stuck in a situation where we have enormous profits being taken in health care but no substantial feedback of resources to support this research.

I think the heart association as well as other medical research organizations suffer because of an attitudinal problem that's prevalent these days in the community, from government on down.

Q. That would include private industry as well?

A. In a -- I think that's generally true, although perhaps it's fair to say that private industry is perhaps the most solid supporter of research these days, and in terms of growth of dollars to research, but their research interests, of course, tend to be much more focused and usually have certain commercial elements to it that get away from some of the basic research aspects that we need to have to answer

questions such as you are addressing.

Q. When you served as president of the organization, that was the Minnesota affiliate?

A. Uh-huh.

Q. Would you be aware of those large corporate or government sponsors who provided funds to the American Heart Association?

A. Yes. I think it's probably fair to say there were no government dollars that went to the American Heart Association and that's probably still true. If there is, it's for very special programs unrelated to general sort of research. I could be in error there but I don't think so. Certainly private donors, large corporations were the major and continue to be, my understanding, the major supporters of basic research that's undertaken by the American Heart Association and other research bodies that deal with cardiovascular disease. I think that among the least active supporters of such research are health insurers and various health maintenance organizations and other groups of that type that promote their activities in terms of hospital care and health insuring but are rather poor supporters of research, of basic research. They may support some commercially oriented research but not basic research

of the type that's necessary to address the scientific certainties that you are alluding to.

Q. Are you aware of any financial support to the American Heart Association in Minnesota by the tobacco industry?

A. I'm not aware of any, no.

Q. The American Heart Association, as you've explained, has limited funds to support its own research; is that what you are telling me?

A. That's correct.

Q. Does the American Heart Association in informing its physicians and public information rely on studies conducted in the medical community outside its own studies?

A. Yes.

Q. And is that a reasonably reliable method to determine their public relations and public education positions?

A. I think it has to be. I think you would have to take information from wherever it's available, screen it to be sure that it's both ethically sound, scientifically sound and what have you, and then determine what level of evidence it provides you in conjunction with all the other materials you have.

Q. I would assume, sir, that that evaluation of

studies to determine ethical and scientific soundness and basis is something that the heart association would routinely do before formulating any positions or public information?

A. I believe that's correct. To the best of my knowledge that's usually done through task forces, if you will, or committees of scientists appointed by the organization. And I shouldn't just say scientists, because not infrequently lay people are also included. I think that's actually more common than not in evaluating this material.

Q. I just wanted to confirm the time frame so we have it. According to your curriculum vitae, you were president from 1991 to 1992? Just to refresh your recollection.

A. Okay. Fair enough.

Q. And you have served on the board of directors of the Minnesota affiliate of the American Heart Association since 1984; correct?

A. Yes, although that is an error. I notice it says "1984 to present." That is not correct. It would be 1984 to about 1994.

Q. Okay.

A. Get that changed.

Q. Was there any particular reason why you went off

the board in 1994?

A. No. It's just standard practice that within a year or two of completing your presidency role, if you will, or whatever role that one filled, that there was about a 10-year time frame of tenure there, and I think that's fairly standard.

Q. Did you enjoy that work?

A. Very much.

Q. Dr. Benditt, during the time you were serving on the board, that 10 years from 1984 to 1994, do you recall what the American Heart Association's position was with respect to the relationship between cigarette smoking and heart disease?

A. Yes. The -- Between 1984 and 1994, the organization clearly felt that smoking was a risk factor associated with cardiovascular disease and that by modifying smoking both in the home, and in those years particular emphasis in the workplace, one could modify or more specifically reduce the risk of occurrence of the complications of cardiovascular disease.

Q. Is that a position you agreed with, sir?

A. Yes.

Q. And do you still agree with that position?

A. Yes.

Q. And is that still the position of the American Heart Association?

A. To the best of my knowledge.

(Plaintiffs' Deposition Exhibit 3801 was marked for identification.)

BY MS. FLYNN PETERSON:

Q. Dr. Benditt, showing you what has been marked as Exhibit 3801, would you please review that document, sir. I will ask you whether you recognize it and then ask you to identify it for the record once you have had a chance to review it.

A. Yes, I recognize this to be a statement on smoking and cardiovascular disease for health care professionals published in the journal Circulation. Circulation is a journal of the American Heart Association and this article is dated November 1992.

Q. Is that a peer-review article or peer-review journal, I should say?

A. This is a position statement. The position statements of the American Heart Association, and this is to the best of my knowledge because this is a national -- part of the national American Heart Association system, so the peer review of these is done through a variety of both scientific, educational, lay, public relations people.

Q. Let me just make sure you are answering the question I asked. Is the journal Circulation, perhaps I wasn't clear, do you know whether that's a peer-review journal?

A. Oh, as a general rule the articles published in Circulation are all peer review.

Q. All right. Now you were explaining specifically with respect to this publication which says it's AHA, American Heart Association, correct, medical slash scientific statement and position statement.

A. Correct.

Q. Now were you answering a question explaining what the --

A. Yes.

Q. -- that was peer reviewed?

A. Yes. I was specifically referring to the types of position statements that are --

Q. Okay.

A. -- from time to time published in this journal. The journal is a very highly regarded scientific journal. The articles in it tend to be broken down as in many journals, into scientific, if you will, peer-reviewed articles that are submitted by independent investigators for peer review by various of their peers, other scientists, and if deemed

scientifically solid can be published in Circulation. There are other articles which are more editorial articles that are invited by the editors which are not peer reviewed quite as critically because they are meant to provide a personal or group perspective, and then there are other articles such as this which are editorial statements including some scientific materials to support those statements that are then approved by the, presumably, board of directors or board of trustees of the American Heart Association as being, at least at that point in time, the position of the organization vis-a-vis whatever topic it is, in this case smoking and cardiovascular disease.

Q. And in fact that was the case in this article. I believe if you look at the lower left-hand column, the very first column, it does say that this was approved by the American Heart Association steering committee on May 15, 1992. Is that the process you were just describing to us?

A. Yes, although I wouldn't be surprised if this particular one also would have been approved by the board of directors or board of trustees of the organization. In other words, which is a higher level.

Q. Okay. Why?
A. Well, I think that when one comes out with statements that are so important in terms of public -- potential public-health impact, particularly in controversial areas, the organization needs to both make sure that it's scientifically accurate as well as protect its reputation.
Q. Dr. Benditt, I'd like to refer you to some portions of that article. As you look at the article, and I'm in the first sentence of the article in the first paragraph on page 1664, do you agree that cigarette smoking "substantially increases the risk of cardiovascular disease, including coronary heart disease, stroke, sudden death, peripheral artery disease, and aortic aneurysm"? Do you agree with that statement, sir?
A. I think the word "substantially" is a qualitative term, but apart from that, the rest of it is accurate in my estimation. The term "substantially" is a word that I think could be left out because there are risk factors for each of those diseases and the relative increments of risk associated with each of those differs. So if one looks at each of those disease conditions specifically, one will see that the term

"substantially" becomes questionable, but the rest is a reasonable statement.

Q. Do you agree that "The overwhelming and consistent evidence supporting a causal role of smoking in cardiovascular disease derives from large numbers of observational analytic studies both case control and perspective cohort, in the United States, Europe, and Japan that include more than 20 million person-years of follow-up"? Would you agree with that statement?

A. This statement is actually a very interesting statement and I don't agree with one element of it. I think that it's fair to say in science that one cannot come up with causation of a disease process based on observational analytic studies. It is an inherent conflict there. Observational analytic studies are basically what they are, they are observational analytic studies. They are not scientific valid assessments of cause. It certainly, there is no question, creates a relationship or an association of risk factor here and I don't think anybody would reasonably argue with that. But the term "causal role" is kind of a bad term because it implies that -- an insight that frankly we don't have.

Q. As I understand your testimony, then, you believe there is no reasonable basis to argue that cigarette smoking is not related to cardiovascular disease?

MR. BORMAN: Object to the form.

A. I'm sorry, could you put that more simply for me?

Q. You said that you don't -- you are testifying here today that cigarette smoking does have a relation to cardiovascular disease; correct?

A. Yes.

Q. That it is a risk factor?

A. Yes.

Q. And you believe that nobody could reasonably argue that it is a risk factor, argue against it being a risk factor?

A. Yes.

Q. And as I understand it, you do not believe that observational analytic studies, both case controlled and prospective cohort studies, can give you any information about cause?

A. In the specific context of smoking and cardiovascular disease, that's my belief.

Q. Are there other types of aspects where you believe those types of scientific studies can give

information relative to cause?

A. It would be possible to hypothesize situations where there was a single element involved and in which the control population did not have that element and that no other factors participated. I think that that would be an extremely difficult kind of study to put together in the human population. It might be doable in a very well-controlled animal population of experiments, but the difficulty even there is that controlling for all related activities or related diseases or related influences is extremely difficult. And when we do scientific studies and we submit them for peer review, it's amazing how the reviewers just tear them apart because we haven't controlled for this or controlled for that or whatever. And when you try to do something like that in a public-health domain, you can envision all the incredible numbers of influences that occur.

So, I would say it's possible to do it hypothetically, to come up with such an experiment, but I think in this setting we come up with risk factors and maybe associations, and that's important.

Q. So what you are arguing about is the strength of the risk factor and the strength of the association?

A. The strength of the risk factor can probably be quantitative, but the causal nature versus other elements of health that occur in that population is really the issue that I think has not been clearly dealt with. We know that there are many factors that result in cardiovascular disease, smoking being one of them.

Q. Is it a substantial factor?

A. I dislike the term "substantial" because I don't know what that means. I think we know that there are factors and there have been quantitative estimates of the relative strengths of those factors, and if we looked in the literature, some of which is cited in -- in various of the probably papers that are sitting in front of you, the strength varies depending on which risk factor you are looking at.

Q. Dr. Benditt, if you accept the definition of "substantial" as being a fact that is more likely true than not true, would you agree that cigarette smoking substantially increases the risk of cardiovascular, including coronary heart disease, stroke, sudden death, peripheral vascular disease and aortic aneurysm?

MR. BORMAN: I'll object to the form of that question.

A. I just sort of got lost there. Could you repeat or read back that question?
Q. I can repeat the question.
If you accept the definition of "substantial" as being more likely true than not true, you previously told me you dislike the term because you don't know what the definition is so I'm asking you to accept that definition. Can you do that, sir?
A. Yes.
Q. If you accept that definition that cigarette smoking substantially increases the risk of cardiovascular disease?
A. Yes.
Q. And would that include coronary heart disease, stroke, and peripheral vascular disease?
A. Yes.
Q. Would it also include sudden death and aortic aneurysm?
A. Sudden death, yes. The aortic aneurysm, I don't know.
Q. Do you agree under the section of Exhibit 3801, "Quantification of Risk," do you agree that current cigarette smokers have a 70 percent increased risk of fatal coronary heart disease?
A. That's a number that's commonly stated. That

would be a risk, increased risk of 1.7, which is the number that is most commonly provided in the literature.

Q. Would you agree that the overall incidence of nonfatal coronary heart disease as well as sudden death is twofold to fourfold higher in cigarette smokers? Again, doctor, I'm just referring again to the first paragraph under "quantification of risk."

A. Yes. These are risk statements that I would have no reason to argue against.

Q. And again proceeding further, do you agree there is a strong and consistent dose-response relation of smoking with coronary disease?

A. The American Heart Association uses the term "strong and consistent dose-response relation."

Q. Do you agree with that?

A. That's not something that I can say that I have personal experience with. I can agree with -- with what they have cited in the literature.

Q. Okay. Would you agree that there is strong evidence that cigarette smoking increases the risk of stroke?

A. Increases the risk of stroke, and cigarette smoking does do that, yes.

Q. Would you agree that cigarette smoking is the

strongest risk factor known for atherosclerotic peripheral vascular disease?

A. No, I don't think that's proven.

Q. Would you agree that smoking cessation yields significant reductions in coronary heart disease?

A. I think that smoking cessation has been associated with a reduction in mortality associated with coronary artery disease.

Q. Dr. Benditt, do you agree that along with cigarette smoking, hypertension and elevated blood cholesterol are major independent risk factors for cardiovascular disease?

A. Yes, they are.

Q. Do you agree that cigarette smoke is clearly toxic to vasculature?

A. I don't agree with that. I know that the American Heart Association has made that statement in this article but there are other studies, inhalation animal studies in animals that have not really clearly demonstrated the occurrence of atherosclerosis, so I think that one may want to quibble here a little bit by saying it may be toxic but it doesn't necessarily imply that the toxicity that occurs results in atherosclerosis, which is the sort of sine qua non of coronary artery disease that

we are talking about anyway, so --

Q. Would you agree that endothelial injury is an essential feature of vascular disease induced by cigarette smoking?

A. That has been reported.

Q. Do you agree that current knowledge provides health care professionals with overwhelming evidence of the cardiovascular disease hazards of cigarette smoking?

A. Hazards in terms of risk factors are clearly demonstrated in current studies, yes.

Q. Do you agree with the American Heart Association's recommendation in its 1992 article that health care professionals such as yourself should vigorously exercise influence to decrease smoking rates in the United States?

A. Yes.

Q. I'm a little disorganized here.

A. Thirty-eight hundred one pieces of paper so far.

Q. Thank goodness you and I haven't had to go through each of those today.

(Plaintiffs' Deposition Exhibits 3802 to 3805 were marked for identification.)

(Recess taken from 9:25 to 9:32 a.m.)

BY MS. FLYNN PETERSON:

Q. Doctor, showing you what has now been marked as Plaintiffs' Exhibit 3802, again I would just ask you for purposes of identifying for the record, would you review the document and then tell us what that document is.

A. This document is again a publication of the American Heart Association published in the journal Circulation in August 1992, and is a position statement of the organization related to environmental tobacco smoke and cardiovascular disease.

Q. Again, Dr. Benditt, I'm just going to ask you whether you agree with some of the positions stated in this article. Do you agree that cigarette smoking has a significant effect on the health of Americans and is a major cause of cardiovascular disease?

A. I agree that cigarette smoking has a major impact on health of Americans. If you delete the term "cause" from your statement, I think that we could agree with most of it.

Q. So you disagree that cigarette smoking is a major cause of cardiovascular disease?

A. Well I think we simply don't know the answer to that question at this time. We know that it's a risk factor and we need to know more, we need to learn

more about its role as a, if you will, cause, so I think that's why I'm quibbling about that aspect of your statement.

Q. What more would you need to know about cause?

A. Well I think that scientific studies that have looked at the relationship of cigarette smoke and toxins, if you will, the other chemicals that are in it, to the causing of vascular disease and the ultimate development of atherosclerosis and coronary artery obstruction, these studies are not conclusive and whereas we have got very good inferential data based on risk-factor analysis, some of which we have already discussed this morning, we don't have information that specifically says in the absence of everything else cigarette smoking itself causes vascular disease and of the type that causes coronary artery disease. This is an important distinction because there are experimental studies that basically haven't shown a direct relationship, particularly inhalation studies in animals. So that doesn't mean that it's not a cause; it just means that we don't know. And that gets back to the ongoing search for resources to do research.

Q. Would you agree that environmental tobacco smoke produces acute effects on cardiovascular function in

humans?
A. Yes, that appears to be true.
Q. Would you agree that cigarette smoking is a major preventable risk factor that promotes atherosclerotic peripheral vascular disease?
A. We don't know the answer to that one.
Q. So you disagree with that statement?
A. Yes. I think it's a major, or a risk factor, I'll say. The term "major" again is sort of semi-quantitative. I don't even know what that word means in this context. But it's a risk factor in -- that is associated with coronary artery disease in its manifestation. As a cause of atherosclerosis, I think it gets back to my first concern that we can't say that unequivocally.
Q. Do you know what the American Heart Association means when it uses in its position statement the term "major"?
A. No, I don't.
Q. While you were on the board of directors of the American Heart Association, did you ever take the position in opposition to any -- I just was pausing while you were checking your pager, doctor.
A. Appreciate that.
Q. Do you -- Do you need to respond to the pager?

A. No.
Q. Let's start over with the question.
While you were on the board of directors or serving as president of the American Heart Association here in Minnesota, did you ever go on record as opposing any of the positions taken by that organization relative to cigarette smoking and cardiovascular disease or coronary artery disease?
A. No.
Q. Do you agree with the American Heart Association's Council on Cardiopulmonary and Critical Care's conclusion that "environmental tobacco smoke is a major preventable cause of cardiovascular disease and death"?
MR. BORMAN: Where are you reading that?
MS. FLYNN PETERSON: The last paragraph of the article, page 701, first sentence.
MR. BORMAN: Thank you.
MS. FLYNN PETERSON: You're welcome.
A. Well I guess my view of this would be that were I on the council, I would have said that it certainly is a preventable factor that is -- that can help to diminish the impact of cardiovascular disease and cardiovascular death. If I were on the council, I would have quibbled with the term "is a known cause,"

and I think that, unfortunately, from the perspective of actually getting to the bottom of this problem, by making statements like that it implies a level of knowledge that then people assume, well, we don't need to do any more research in this area because these guys know what's going on, when the scientific literature is really not solid in this particular area of cause. And I think that it's one thing to say that in a public relations piece that's going out into the community to try and get people to change their habits, but to make that statement in a journal article that's presumably peer reviewed, although this is a position statement so it's peer reviewed in a different way than other scientific articles, I think I would have disagreed with that word.

Q. Showing you what has been marked as Plaintiffs' Exhibit 3803, Dr. Benditt, that is one of the types of public relation pieces you have been referring to; correct?

A. Yes, it appears to be, from the American Heart Association.

Q. And this particular one is American Heart Association publication entitled "Smoking and Heart Disease," just for the record.

A. That's correct.

Q. Now I obtained this copy by going to the Minnesota affiliate of the American Heart Association. I'm assuming that the Minnesota affiliate distributes publications of the American Heart Association?

A. Yes, that's correct.

Q. So the American -- the Minnesota affiliate doesn't just have all of its publications for Minnesotans, are just local. They also rely on the national publications; correct?

A. Yes, and I believe perhaps the majority of the publications that are distributed are provided from the national organization.

Q. And I note this particular pamphlet, if you look at the bottom of the inside, I believe it's the first page, maybe where your hand is just covering, does indicate some dates. It shows 1986, 1992 and 1995. Do you know what those dates refer to?

A. I would assume that this article or pamphlet was revamped on each of those times and presumably updated, and that's the copyright designation for those years.

Q. Do you agree with this pamphlet as it states in the first sentence: "For years the link between cigarette smoking, lung cancer and chronic lung

disease has been well documented and well known." Do you agree with that?

A. The link? Yes, I agree.

Q. Do you agree with the third sentence, "Cigarette smoking is also a major cause of heart and blood vessel disease"?

A. That gets back to my previous problem where I say that cigarette smoking is a risk factor of heart blood vessel disease. In this kind of article, I don't quibble so much with the use of a more -- of the term "cause," and I put that in quotation marks, only because this is trying to promote a concept in the lay public and the lay public sort of needs to have it put in reasonable terms that it will impact their life, and if you quibble too much you are not going to impact their life. So that's why it's used here but I don't think it's scientifically valid.

Q. In your opinion, Dr. Benditt, is the American Heart Association's work to get the public to stop smoking important work?

A. Very.

Q. If you look at the section on atherosclerosis, do you agree in the second paragraph that: "Hardening of the heart's arteries (coronary arteries) and of the main artery (aorta) occurs more

often in smokers than nonsmokers"? Do you agree with that statement?

A. Yes, that statement is accurate because it implies there is a risk-factor association.

Q. And do you agree with the next sentence: "And when it occurs, it tends to be more severe in smokers"?

A. I don't have any reason to disagree with it. I don't have any personal experience that compares the severity issue, and I don't have any personal knowledge of studies that compare severity because I'm not quite sure what they mean by that. Do they mean that there is more clogging of the arteries, or do they mean that the manifestations of the disease result in more bad or worse outcomes? And I guess I would need to know what they are getting at.

Q. Okay. The section on smoking and peripheral vascular disease, do you agree with the statement: "Smoking is a major risk factor of peripheral vascular disease. Smokers get this disease more often and more severely than nonsmokers"?

A. Certainly it appears to be true smokers are afflicted with peripheral vascular disease more than nonsmokers and that smoking is a risk factor for peripheral vascular disease. The term "major" again,

you know, I just don't know what that means relative to other risk factors.

Q. Okay.

A. And in a public-health-promotion article such as this, I think terms like that are suitable because they have impact. I think in the context that we are discussing the role of cigarettes and vascular disease, we need to be careful about terms like that.

Q. Doctor, showing you what has been marked as Plaintiffs' Exhibit 3804, again would you please review that. And I will ask you whether or not you recognize that as one of the scientific positions of the American Heart Association.

A. This article numbered 3804 I don't personally recognize as a publication of the American Heart Association. It does say at the top "AHA Scientific Position," so I guess I could accept that but it doesn't appear to be on standard AHA stationery with their usual logo and all the peripheral things I look for to see if it is in fact from them, but I'll accept it is if you say so.

Q. I will tell you I was provided with it by the Minnesota affiliate. I also recognize it's not on any type of stationery so I was curious as to whether

you recognized its form.

Doctor, referring to Exhibit 3804, would you agree with what is stated on that exhibit that cigarette smoking is the most important preventable cause of premature death in the United States?

A. I wouldn't agree with specifically the way its written. I would change it to say that cigarette smoking is the most important preventable risk factor.

Q. Would you agree that cigarette smokers have a greater risk of developing chronic disorders such as atherosclerosis?

A. Yes. All of the -- Oh. All of the statement in terms of greater risk of developing atherosclerosis is certainly true in my experience.

Q. And also do you agree with the statement "many studies detail the evidence that cigarette smoking is a major cause of coronary heart disease"?

A. I think that that misstates the evidence, that the evidence is that it's a major risk factor in the development of coronary artery disease, again using the term "major" in a public health as opposed to a quantitative sense, scientific quantitative sense.

Q. In the second section of that scientific position where it says specifically, "What are the

risk factors for heart attack?" I will ask you do you agree, Dr. Benditt, cigarette/tobacco smoke, high blood cholesterol, high blood pressure and physical inactivity are the four major independent and modifiable risk factors for coronary heart disease?

A. Yes, this I believe to be true. It's important to underline the word "modifiable" because we know that there are many, many other risk factors. Some have published over 200 risk factors, many of which we can't modify because they are inherent to our genetic makeup or whatever, but there are others that are modifiable, perhaps such as stress and things of that nature. But these are conventionally listed as the most important modifiable ones.

Q. And do you agree they are independent risk factors?

A. That's my understanding from the literature, yes.

Q. Dr. Benditt, showing you what has been marked as Plaintiffs' Exhibit 3805, does that, sir, appear to be a public advocacy position statement of the American Heart Association?

A. Yes. And this has a copyright of January 1997 by the American Heart Association at the bottom.

Q. And that has to do with cigarette advertising?

A. Correct.
Q. Are you familiar with this advocacy position of the American Heart Association?
A. I am.
Q. Do you agree with it, sir?
A. The advocacy position I agree with, correct.
Q. Dr. Benditt, I'd like to talk to you about your professional practice at the University of Minnesota. Do you -- Are you involved in treating patients?
A. Yes.
Q. In diagnosing patients?
A. Correct.
Q. Do you have specific clinic hours on a weekly basis?
A. Yes.
Q. How many clinic hours do you have on a weekly basis?
A. Minimum of six. May I clarify?
Q. Sure.
A. The -- By "clinic hours," just for purposes of definition, that's where patients make appointments to see you and talk about problems in the clinic. The rest of the week might be construed also as being clinical or clinic hours in the sense we see patients

most of the rest of the week and take care of specific problems but not in a conventional clinic atmosphere. Does that make sense?

Q. Sure.

A. Okay.

Q. Would those include making rounds at the hospital?

A. Correct, making rounds at the hospital, seeing patients in an outpatient setting and undertaking specific treatments or diagnostic procedures as we have scheduled.

Q. And as a specialist consulting with other physicians?

A. That too, yes.

Q. What facilities do you practice medicine at?

A. Basically I practice primarily at Fairview University Medical Center and St. Cloud Hospital and Central Minnesota Heart Center in St. Cloud. I also have a consulting role at Fairview Southdale Hospital, at Hennepin County Medical Center, although that's rather infrequent compared to the others, and at the VA Medical Center in Minneapolis.

Q. When you say Fairview University Hospital, do you go to each of the campuses? For instance, do you go to Fairview Riverside, Fairview Ridges, or

primarily at the university facility?
A. Primarily at the university facility, although we do see patients at the Riverside campus.
Q. At the clinic there or the hospital?
A. In the hospital primarily for my purposes.
Q. And then do you also have a component of research to your daily practice or weekly practice?
A. Yes. A large part of my ultimate responsibility is furthering education and research and the amount of time that's put into that, of course, will vary from week to week depending on clinical responsibilities, taking care of patients, but over the course of the year we try to make a fairly high priority to that and probably accounts, I would say, for something in the range of 30 percent of my yearly professional time.
Q. Does that include research you are doing as well as supervising research of other individuals?
A. That's correct.
Q. And then would it be a fair estimate that the other 70 percent is clinical practice?
A. That's correct, as long as you allow me some vacation time.
Q. In your clinical practice, do you include -- do you do any didactic teaching?

A. I do.
Q. Do you include both your clinical and didactic teaching in that?
A. I'm sorry, could you clarify that?
Q. In that 70 percent, does that include teaching or is teaching in the 30 percent?
A. I understand. The teaching is predominantly in the 30 percent but I also do a lot of, if you will, after-hours teaching, weekends, evenings, whether they be in town, out of town, teleconferences which aren't included in the sort of standard work, you know, workweek.
Q. Would that include presentations at medical meetings and scientific meetings?
A. Exactly, yes.
Q. But you also have a component to your particular practice where you are teaching medical students and residents and fellows at the university, aren't you?
A. That's correct.
Q. And that would be time that you have included in your 30 percent.
A. It gets a little blurry because certainly the education, the didactic education and the research would be in that 30 percent. For many of our postgraduate fellows and residents, much of the

teaching is part of the clinical activities; in other words, the teaching is undertaken at the same time that we are seeing patients or undertaking diagnostics or treatments, treatment studies, and so as you can imagine, the timing gets a little blurred because many of our teaching commitments are actually training in a more practical day-to-day clinic atmosphere type of training rather than a didactic lecture.

Q. Your particular practice, given that you are in a teaching hospital, would be that when you see patients, most often you are seeing them in conjunction with residents or medical students or fellows?

A. Well that certainly was the way it used to be. That is becoming less and less common as another national trend has sort of evolved into where there is less health care training in the medical profession than -- or less interest in it than there was, say, five or 10 years ago and -- excuse me -- for example, even at the university campus now the support for postgraduate specialty training and cardiovascular disease has dropped I would say roughly in half compared to what it was five to six years ago, and so more and more the professorial, if

you will, practitioners are doing basically the same work that -- that our colleagues in private practice are doing, and in our outreach environment where we provide service in outside communities, in my case predominantly in St. Cloud, we have virtually no teaching, if you will, commitment at that time. Maybe I should say teaching opportunity. So things are changing.

Q. And as a specialist, Dr. Benditt, you have had a private-practice-like situation for patients for a number of years, haven't you?

A. Yes. It will be 19, almost 20 years in this city following my training.

Q. And in that capacity you are called upon by other physicians in the community to consult with them when patients have electrophysiological problems?

A. Electrophysiological problems and related conditions that pertain to heart-rhythm disturbances in a broad sense, correct.

Q. Is it fair to say that you have limited your practice for a number of years to heart-rhythm disturbances as it relates to cardiovascular disease?

A. I have tried to limit my practice in that regard, although it's not feasible to do it

exclusively because the patients who have heart-rhythm disturbances have multiple other things going on at the same time. They may be diabetics, they may have had heart attacks, they may have had various heart muscle disease, they may have un -- conditions unrelated to the cardiovascular system. And while I may not consider myself to be an expert in those areas, I still try to identify those problems and provide access to appropriate experts as -- as necessary. So, my practice may have allowed me to see a patient because of a heart-rhythm disturbance but not infrequently I will in one way or another participate in that patient's other health problems over time.

Q. Is the common denominator for all the patients you see a heart-rhythm disturbance, either ruling that out or diagnosing and treating that condition?

A. In a broad sense I would say that probably covers 80 percent of the practice and then roughly 20 percent will be general cardiovascular problems that people have asked me to see for whatever reason and, as I say, I may not consider myself to be an expert in that area but I do consider it my responsibility to at least find out roughly what the problem is and try to find a colleague or other more expert

individual to help with that patient's care.
Q. So you would refer those patients to other subspecialists?
A. Indeed, yes.
Q. When a patient comes to you for medical diagnosis or treatment and they are a smoker, what do you counsel them with respect to smoking?
A. As a general rule, I try to counsel patients to stop or at least minimize their smoking habit and I also look for other risk factors for disease and try to get them to modify those as well.
Q. How long has that been your practice, sir?
A. As long as I can remember. Probably dating back to when I first started to deal with cardiovascular disease in the early to mid-'70s.
Q. And why do you do that?
A. Well I think that I know from my training and from reading that risk factors that aggravate vascular disease are likely to be causing problems for my patients and my job is to provide them the best advice I can, try to minimize the impact of any disease they have, and in order to do that we try to minimize other conditions that might adversely affect their underlying disease.
Q. And is cigarette smoking a risk factor that

aggravates vascular disease?

A. It certainly is a risk factor that aggravates the manifestations of vascular disease, yes.

Q. Do you smoke, sir?

A. No.

Q. Have you ever smoked?

A. I think I smoked a pipe for roughly five years. I was not a cigarette smoker.

Q. Have you ever worked for the tobacco industry before this case?

MR. BORMAN: Object to the form of the question.

A. I don't work for the tobacco industry now nor previously have I ever worked for them. I'm an independent individual so not -- not working for them now, nor have I ever.

Q. Have you ever testified in a case on behalf of the tobacco industry before this litigation?

MR. BORMAN: Same objection.

A. No, not to my knowledge.

Q. Have you ever participated in any research that has been supported in full or in part by the tobacco industry?

A. Not to my knowledge.

Q. Have you ever received any grants from the

tobacco industry?

A. No, I have not.

Q. Have you ever been asked to do any research by the tobacco industry?

A. No, I have not.

Q. Dr. Benditt, when were you first consulted about being an expert in this litigation?

A. I would have to give you a guess, but I would say probably a year and a half or two years ago.

Q. Do you --

A. I don't exactly remember the date, I'm sorry.

Q. Do you recall who contacted you initially?

A. I was contacted initially through an organization which I think is called the University Consortium, which basically operates as a clearinghouse for individual experts and -- at the university, and the contact was through the firm of Dorsey & Whitney but I can't give you the name of an individual.

Q. Tell me about this University Consortium, what do you understand that to be?

A. Basically my understanding is that it's simply a listing of various we will call them experts, using that term loosely, at the university who know about different fields of maybe medicine, arts and probably

whole host of things, who can be available for private corporations to consult with or matters such as this or individuals who are interested in supporting research and looking for somebody who happens to be interested in that field that they are interested in, you know, things of that nature. So it's basically a telephone directory, as best I can put it, with your specific areas of interest associated with it.

Q. Do you recall how that contact was made initially? You don't recall who made it.

A. Just by telephone conversation.

Q. What were you asked to do?

A. Basically just asked to review literature related to the scientific -- status of scientific knowledge in regard to smoking and cardiovascular disease in terms of risk factors, the issue of cause -- excuse me -- and related matters and be available to discuss those issues both initially and -- with various attorneys and subsequently in court if necessary.

Q. Were you provided with literature?

A. I was provided with literature and also used my own resources to gather literature.

Q. The literature that you were provided, does all

of that literature appear as references to your opinion in this case?

A. I don't believe so. I think that in terms of the document that I provided, the expert-testimony document I think it's --

Q. Your expert report?

A. -- that cites a number of references, some 25 or 30 references perhaps, but I have perhaps another hundred references at my disposal, or maybe even many more, and I may have more as I learn more about the subject, and so I didn't cite all of those.

Q. Do you have a separate file where you maintain those references?

A. No. I have a whole series of file cabinets in my office, though, that relate to cardiovascular disease and its manifestations. I would say two or three large file cabinets. But these days we also do a lot of research on Medline on the computer and we just download it and look at it on the screen and then it vanishes, but we can also re-access it. It's very difficult to keep all the paper around that one needs or one might wish to look at.

Q. If you were asked to collect the references that you have reviewed in formulating your opinions in this case from the time you were consulted to the

present time, the time you were first consulted, how would you do that?

A. Well the first thing I would do would be to go back to the Medline list just related to tobacco and cardiovascular disease and that alone probably provides a list of two or three hundred references, I'm guessing, and from those I could check off ones that I recognize that I've looked at and I may find others that I should have looked at that I would then pull out to read. And of course the Medline list changes as each month passes, although frequently they update it so there is probably new terms coming out on a fairly regular basis.

Q. When you were first consulted approximately a year and a half ago, did you begin doing research right away? By "research" I mean reviewing literature at this point.

A. I think that's an accurate statement. I had already, I thought, a fair knowledge base to work with because obviously this topic is part of my day-to-day work and has been for almost 20 years or maybe more than 20 years. So I had a fair amount of information in my own personal files as well as textbooks that -- that I think are fairly standard that have been cited, so I reviewed a lot of that

material as time went by. I can't say I sat down and spent, you know, set aside days just to do that, but as time went by, starting roughly from then, to review what I had, new materials I hadn't paid attention to up to that point.

Q. Did you do that in order to form the opinions that you would express in your expert report in this case?

A. That's correct.

Q. Now you said you were provided with some literature to review initially. Was that provided by some attorney at Dorsey & Whitney?

A. The literature that I was provided was based -- I can't remember exactly who gave it to me but it was based on discussions that I had initially with the attorneys regarding this case and some of the literature that came up was usually just references that were in standard articles and maybe I read the standard article but hadn't really searched the primary source, so we got some of those articles out, the primary source articles, but also some review articles that I hadn't been aware of.

Q. If you were asked to put together that list of references that you have been provided with from attorneys in this litigation, would you be able to do

that?

A. Well I think that most of the ones that I had been provided are listed in the expert document, at least up to the time that that was written.

Q. Uh-huh.

A. And that's not to say all of them. I'd say that there is probably a third of them that are listed there.

Q. Where are the other two-thirds?

A. The other two-thirds are probably in my files or off Medline.

Q. Would you be able to get those if you would be able to do that?

A. Uh-huh.

Q. Okay.

A. Yes.

Q. Now it sounds, from what you said, that you have continued to receive articles from the time you have written your expert report?

A. I wouldn't say "continue" like it's a continuous process. I think I received articles a couple times in the course of this two year -- most of the articles I have read have been materials that I searched out myself.

Q. And have those materials that both you have been

provided with and those you have searched out yourself, have you reviewed those either for expressing your expert opinions or in preparing for your deposition today?

A. Both, I would think.

Q. And so those articles would and the information from them have at least formed some basis for your opinions in this case?

A. Correct.

Q. When you were first contacted you received a telephone call. Was there a meeting that occurred sometime after that telephone conversation?

A. Yes. I believe it was a meeting probably within a month or so after that.

Q. Do you recall who you met with?

A. I don't recall the names of the attorneys. It was not anybody in this room, but it was in this building.

Q. The meeting took place in this building?

A. Yes, I'm pretty sure that is correct.

Q. Have there been more than that one meeting?

A. I think I have had no other -- this -- no other meetings in this building. We have had, I would say, three meetings in my office and maybe two meetings at sites in the Twin Cities' area that just happened to

be more convenient to me at the time.
Q. What sites were those, Dr. Benditt?
A. One was at -- near the airport because I was I think coming or going or something like that, and another one was in -- at a hotel in the western suburbs because I was at another meeting in that vicinity.
MS. FLYNN PETERSON: Would you like to take a break?
THE WITNESS: Why don't we do that, if you don't mind.
(Recess taken from 10:13 to 10:23 a.m.)
BY MS. FLYNN PETERSON:
Q. We were talking about the various meetings that you recall having had with attorneys in this matter. Now have you told me, doctor, about all the meetings you recall having? There was one here initially at the law firm of Dorsey & Whitney, you thought two or three at your office and others at other locations throughout the Twin Cities.
A. I believe that's accurate.
Q. When did the last meeting you had occur?
A. Friday past.
Q. Do you recall who was present at that meeting?
A. Yes, everybody at this table.

Q. Everyone here. Anyone else other than the attorneys who are present here this morning?
A. It's -- There was one other attorney.
THE WITNESS: Was it Betsy? Is that correct?
MS. FARRAR: Uh-huh.
A. So there was -- that was the extent of them.
Q. And do you recall anyone who was at any of those other meetings, Dr. Benditt?
THE WITNESS: There was just one other attorney that I recollect and that was from your firm in Kansas City; right? And I've forgotten his name.
MS. FARRAR: Clyde Curtis.
A. Clyde Curtis.
Q. At any time when you have meet with the attorneys at these meetings you have described, have any other experts or physicians been present at the meetings?
A. No.
Q. You told me that you had been provided with some articles, both initially and some from time to time since that time, that you had also reviewed some articles yourself. Have you been provided with any document other than medical articles?
A. The only other documents, I don't know whether

you classify them as a medical article or not, would be the surgeon general's report from 1983 and 1989. I think those are the correct years.

Q. I note that at least I think the 1983 one you cited in your materials and perhaps --

A. I believe that's correct.

Q. -- and I believe the 1989 one as well. So there have been no other art -- documents other than the surgeon's report and the other articles?

A. None that I can recollect.

Q. Other than documents you might have been provided with as far as receiving copies, have any documents been reviewed with you during these meetings where you were not provided copies?

A. I think I understand that question.

The only documents, now that you mention it, that I observed would have been documents related to, for example, appearing here for deposition or maybe documents specific to the global case but not necessarily copies that I had received.

Q. And when you say "documents pertinent to the global case," can you describe for me what you mean?

A. Well I think I saw a document related to the nature of the complaint, if that's the right term, but that's about all. I don't believe I ever went

through it in great detail.

Q. When you say the "document related to the nature of the complaint," do you think you reviewed the complaint in this case, the document that set forth the plaintiffs' claim?

A. I don't think I reviewed it in detail.

Q. But you have seen it?

A. I think I have seen it.

Q. Have you been provided a copy of that document?

A. No.

Q. Have you discussed the opinions that you have expressed in this case with any other physicians or scientists?

A. No, not in terms of the relationship to the case. I certainly over the years discussed the role of risk factors in cardiovascular disease with a variety of people related just to the clinical practice of medicine and -- but not in specific terms related to, you know, presenting an opinion in this case.

Q. Have you discussed the opinions in this case with anyone other than the attorneys you may have discussed it with or any other physicians or scientists, since I understand there have been none, specifically your opinions in this case?

A. No, I don't think so.
Q. Has anyone expressed to you any opinion about your decision to work as an expert witness on behalf of the tobacco industry?
A. I'm sorry, could you restate that?
Q. Has anyone expressed to you any opinions one way or the other about your decision to act as an expert witness on behalf of the tobacco industry in this case?
MR. BORMAN: Object to the form of the question.
A. I don't believe so.
Q. Now we have talked about the articles, we have talked about documents. Have you reviewed any other experts' opinions in this case?
A. Yes. I reviewed the opinion of Dr. Graham.
Q. Uh-huh.
A. And the opinion of doctor -- you will have to help me with the name -- Jonathan --
Q. Samet?
A. Samet.
Q. Now, were you actually provided with written opinions from them, their expert reports?
A. I was provided them to read; I did not retain those.

Q. So were you shown those at a meeting but not provided with copies?
A. That's correct.
Q. Okay. Well is there anything else like that that you were shown at a meeting but not provided copies of?
A. I'm trying to remember. I'm sure that, as you prod my memory --
Q. All right.
A. -- something may come up, but I can't recall anything specifically.
Q. Do you know Dr. Samet?
A. No, I don't.
Q. Do you know of his reputation?
A. No, I don't.
Q. Do you know Dr. Kevin Graham?
A. Yes, I do.
Q. Do you know of his reputation?
A. Yes.
Q. What is his professional reputation in this community?
A. It's very highly regarded, cardiologist.
Q. Do you know him personally?
A. Yes, I do.
Q. How do you know him?

A. Dr. Graham was a trainee at the university a number of years ago when I was on staff and so I knew him both during that training program and subsequently periodically I've seen him during the course of his practice at Minneapolis Heart Institute.

Q. What was his reputation when he was a trainee at the university?

A. Was very bright and very highly regarded.

Q. You reviewed his opinions in this case?

A. Yes, I have.

Q. Have you also reviewed his deposition testimony?

A. No, I have not.

Q. Okay. Have you been told anything about his deposition testimony?

A. I was told that there was a deposition but I don't believe I was provided any details regarding his opinions in that deposition.

Q. So you have not been provided with any information regarding his testimony in this case other than his written report?

A. That's correct.

Q. And I understand his written report, you were -- you reviewed it but you do not have a copy.

A. That's correct.

Q. And you have never had a copy?
A. That's correct.
Q. What is your understanding of what Dr. Graham's opinion is in this case?
A. Based on the expert testimony that he was -- that I read, his opinion was basically very well couched in typical epidemiological materials. By that I mean that he didn't say any more than I think what we have said this morning about the relationship of risk factors to various cardiovascular diseases, and I was impressed actually at -- for the most part how he framed his discussion. I thought it was a -- very cautiously framed and that it dealt predominantly with associations and risk factors which I would expect an epidemiologist, and I think Dr. Graham is to some extent an epidemiologist in his practice. That's how I would expect him to frame it.
Q. Did you agree with the opinions expressed by Dr. Graham?
A. I don't recall all of his opinions at this moment but I thought that my overall sense was that it was a well-written and reasonable opinion and that there might be parts of it that if we went through line by line I might quibble with, but for the most part he presented the associations quite fairly.

Q. As I understand, the only experts, then, who you have had an opportunity to read, review the opinions of is Dr. Graham and Dr. Samet.

Does anyone else come to mind as we are discussing expert opinions?

A. Not at the present time, but if they do I'll let you know.

Q. Okay. Did you agree with the opinions expressed by Dr. Samet?

A. I would have to go over his opinions in detail. If you had a copy, I'd be happy to do that. I can't recall enough of his opinions to make a reasonable judgment.

Q. Okay. And we will do that, doctor. I just want to know at this point in general terms if you did.

Has your review of the opinions of Dr. Graham or Dr. Samet in any way influenced your opinions in this litigation?

A. No, I don't think so. I believe that in many respects, at least in terms of Dr. Graham's view, that we have a very similar tact, but I don't think he persuaded me differently than the way I was thinking.

Q. Other than the medical research that you have already told us about and the opinions of Dr. Graham

and Dr. Samet, have you reviewed any other written materials or computer-generated materials before you issued your report?

A. Well apart from the materials that I talked of earlier and materials that I referenced in the report, I don't -- I cannot think of anything that falls within that general category I can recall.

Q. Have you reviewed any medical records or medical reports for any patients who might be involved in this litigation?

A. No, I have not.

Q. Tell me, how did you go about writing your report in this case?

A. During the course of reading, we had materials that were provided to me and we discussed and we also had materials that I had at my disposal either in my office or off of Medline at a meeting that was held at -- near the airport over the course of about five or six hours. I expressed my various opinions and notes were taken by the attorneys, and it was from those notes that an original draft was made of the opinion, which I then subsequently had to revise, make it sound a little more nicer, and that was basically what you have seen. The process was complete within a few weeks of that initial meeting.

The initial draft to my knowledge, I was -- was destroyed -- I don't have a copy of that -- and I don't have a copy of the notes taken at that meeting.

Q. The meeting at the airport, where specifically did it take place?

A. The Airport Hilton, as I recall, conference room.

Q. And when, to the best of your recollection, did that meeting take place?

A. I'm afraid I don't recall, but it would have been within a month, perhaps, prior to the submission of that expert testimony document.

Q. Am I correct that after this meeting that then the individuals who took the notes prepared the first draft of the report and provided it to you?

A. I think that the -- that somebody was writing as we were talking, so it was predominantly my ideas. Someone else wrote out or typed up, I guess, those ideas and then I had to change them around again to reflect my view of the subject, and that's the second draft.

Q. Did you review the notes before the report was written?

A. No, I did not review the notes.

Q. So you had a meeting, notes were taken, and after the meeting you were provided with a first draft of the report in a typewritten form?

A. Yes, it was in typewritten form.

Q. Did you --

At any time were you provided with a disk where you entered that report on your computer for drafting purposes?

A. No. I did this longhand.

Q. Do you know specifically what types of changes you made to make it nicer, as you testified?

A. Well I think there were a number of statements that I felt were correct but not really well organized and not in an orderly thought pattern, so it was largely a matter of restructuring paragraphs to make it more orderly, -- excuse me -- and then there were some general statements that we had discussed in the meeting that didn't come out quite the way I had said them for some reason and so I changed those to the way I wanted them.

Q. And you made those changes longhand on the form that you were given; is that correct?

A. That's correct.

Q. And then you returned that form to someone?

A. That's correct.

Q. Who did you return it to?
A. I mailed it back to -- I'm not sure whether it was Dorsey & Whitney, or was it to one of the attorneys that -- the other attorneys who were in that meeting?
Q. Did you maintain a copy for your files at that time?
A. No, I did not.
Q. So you didn't have anything to refer to if there was any phone conversation about the changes you made after that?
A. That's correct.
Q. Do you know whether any copies were made of that first draft?
A. I wouldn't have any knowledge of that.
Q. Were you instructed not to make copies?
A. I never keep copies of anything related to these kinds of activities.
Q. Then after you made those changes, what happened next relative to the report?
A. Some days later I received a revised version, which I then went over and found to be an accurate representation of my thoughts.
Q. And with that, did you sign off on that?
A. I believe I signed off on that and I think it

was notarized, if I'm not mistaken.

Q. Did you make any changes in the second copy of the report that you received?

A. I don't recall having done that. I believe there was only one revision after the initial formulation and I'm pretty sure that's right.

Q. When you sent back a draft of changes, did counsel or anyone else call you to discuss the changes you had made?

A. No, I don't believe so. I believe that those changes were made the way I wanted them. I don't think I received any phone call regarding the changes. I may have received a phone call to say there is another draft coming or X version was coming back, but I don't even recall for sure that that happened.

Q. So is it your testimony, Dr. Benditt, that after the report was provided to you and you made changes there was no discussion about the report until it was finalized, about the substance of the report?

A. No, I can't say that because there was -- when I made my changes in the first draft, I think there was a meeting in my office where I pointed out why I wanted that. It was either my office or the telephone. So there must -- there was a discussion,

but it wasn't very -- it was just my saying this was the way I wanted it and everybody was quite -- I mean, that was agreed to.

Q. And who was "everybody," who were those individuals you either met with or had a phone call with?

A. Well as I recollect, and again my -- I'm -- the timing of this is something that I can't quite put my fingers on but I believe that certainly Mr. Curtis was there at the time I discussed the changes and I think Ms. Farrar was there, too, if I'm not mistaken, but that was really the follow -- that was the only meeting we had, I think, or discussion that we had that evolved around the changes I had made.

Q. How long did that meeting last?

A. I would assume it was less than an hour. I don't think, apart from this Friday, we met for more than an hour on very many occasions in my office or over the telephone, so it was less than an hour.

Q. How did you --

How long did you meet on Friday?

A. It was about two and a half hours.

Q. After the --

Again referring to the meeting that you believe occurred after you had made your changes on the first

draft of the report, after that meeting did you make any other changes on the report?

A. No. To my recollection, there was one set of changes only and that the next draft was consistent with my opinion in the matter.

Q. So there was a draft given to you, you made changes, sometime later you had a discussion with attorneys from Shook Hardy regarding those changes, and then after that time you were provided with a copy of the report with all of those changes made; is that your testimony?

A. Yes, I believe that's an accurate description of the state of affairs.

Q. And just so I understand, you do not have in any form any copies of or information regarding the changes you made on the first draft?

A. That's correct.

Q. Do you have a copy of your report to refer to today, doctor?

A. No. I assumed that you might provide one to me if you wanted to go over it.

MS. FLYNN PETERSON: Do you have a copy for him to refer to?

MR. BORMAN: I only have my copy. We can stop and have one made, I'm sure.

MS. FLYNN PETERSON: Why don't we get a copy. I assumed he would have a copy of his report to refer to. He doesn't.

MR. GINDER: Do we have a clean copy in the room somewhere?

MS. FLYNN PETERSON: I don't have a clean copy with me.

MR. GINDER: Do you want to continue with other questions until I come back?

(Discussion off the record.)

(Recess taken from 10:46 to 10:51 a.m.)

(Plaintiffs' Deposition Exhibit 3806 was marked for identification.)

BY MS. FLYNN PETERSON:

Q. Dr. Benditt, we have a copy of your report now identified as Exhibit 3806. You have that before you?

A. Yes.

Q. And I would like to go through your report with a series of questions at this point and so I will ask you certainly at any time you would like to review any portion of the report, please let me know. It's not meant to be a memory test but I want to understand as much as we can about your report here today.

A. That's fine.
Q. We have previously discussed your qualifications and your curriculum vitae. You indicate that you have a certificate of special competency in cardiac pacing. What is that, Dr. Benditt?
A. That's an examination certificate provided by the Society of Pacing and Electrophysiology that deals with the disciplines of cardiac pacing and implantable defibrillators and it's based upon a written examination.
Q. Is it much like a board certification --
A. Correct.
Q. -- without the orals?
A. -- without the orals, correct.
Q. The first portion of your report defines cardiovascular disease. As you review that definition in paragraph one, do you have any additions or corrections to the definition that you have given of cardiovascular disease?
A. No. I believe that that paragraph is reasonably accurate as it stands.
Q. As I understand it, then, atherosclerotic coronary artery disease, cerebrovascular disease and peripheral vascular disease, as you have defined them, are subcategories of the general term

cardiovascular?

A. Correct.

Q. And you believe that those three specific subcategories of disease are the most important in terms of morbidity and mortality in the United States today?

A. I believe that's true, yes.

Q. What do you mean by that, being the most important in terms of morbidity and mortality?

A. Well among the various types of cardiovascular, of which there are others than the three categories that we have mentioned here, those others are less frequent, and although they cause similar manifestations such as heart failure, rhythm disturbances and death, these forms of atherosclerotic disease are more frequent causes of those manifestations in the population. That's what I meant by that.

Q. Okay. Would another subcategory of cardiovascular disease be rhythm disturbances?

A. Rhythm disturbances are a consequence, generally speaking, of some disease process. The reason I say "generally speaking" is, occasionally they occur in the absence of an identifiable disease, but in the vast majority of cases there is a disease process of

which coronary artery disease, atherosclerotic coronary artery disease is one, of course, of the most common ones we see in practice, but others, just by way of example, would be cardiomyopathies, which are diseases of the heart muscle, valvular heart muscle, which are diseases of the valve that manifest as rhythm disturbances or inflammatory conditions that can cause inflammation of the heart, and there are a whole wide range of those.

Q. And the last three that you have just mentioned with respect to other instances where you see arrhythmias, would those also be different subcategories of cardiovascular disease?

A. I'm sorry, "the last three" being what?

Q. When you went through myopathies, inflammatory conditions, are those other subcategories of cardiovascular disease?

A. Yes, they are.

Q. And you agree that for the three subcategories that you have identified; that is, atherosclerotic coronary heart disease, cerebral vascular disease and peripheral vascular disease, you indicate there are a large number of risk factors identified in those disease categories?

A. That is correct.

Q. And smoking is one of those risk factors?
A. That is correct.
Q. You indicate some medical literature has reported an association between smoking and the development of atherosclerotic coronary heart disease, cerebral vascular disease and peripheral vascular disease. Do you have specific medical literature in mind when you make that statement?
A. I was being very general in that regard. The coronary term "cause," which we have seen some examples of already today, is broadly used in literature, but my comment here relates to that broad use as being imprecise.
Q. Your statement further says "no causal mechanism or proof that is direct and convincing has been scientifically established." Would you explain what you mean by that, sir?
A. Well as we alluded to earlier, there is substantial associative literature, epidemiologic literature that associates various conditions with the occurrence of -- of vascular disease, and smoking is certainly among them but certainly others would be included, could be included, have to be considered, such as hypertension, diabetes, genetic predisposition, et cetera. So that in the sense that

there is an association that seems clear. In the sense that A causes B, I think we need more scientific research, and that's really what I was trying to establish, at least in terms of my opinion.

Q. What would satisfy you with respect to cause?

A. Well I think there are recognized methodologies to establish cause. Perhaps the classic is Koch's postulates, "Koch's" being K-O-C-H apostrophe S, and I think we would need to fulfill those postulates in order to establish cause, and there are assigned rigorous scientific ways about doing it.

Typically we would start in animal models. It may be very difficult, if not impossible, to do it in the human but certainly at least we could start off in in vitro models and in animal models and demonstrate that perhaps the issue that we are interested in, in this case tobacco and its related chemicals, causes the disease in the absence of other factors whereas in the control animal it doesn't. And then in withdrawing, you withdraw the aggravating principle, the disease either regresses or stops and then you reinstitute it and it comes back.

The same process, although perhaps more complicated, that we use to demonstrate that certain

bacteria causes -- caused infections, and remember that in the sense that bacteria causes infections, while it was hypothesized for some time, proof requires some substantial research enterprise and a classic example, of course, that pertains to Minnesota is streptococcal infections in which Minnesota led the way in identifying -- researchers in Minnesota led the way in identifying in the 1930s and '40s and '50s. So in a nutshell, I think that's the kind of research we need to support.

Q. What are Koch's postulates with respect to cause?

A. Well basically, as I said, you have to -- first of all, you have an identified hypothesis and essentially you have to demonstrate that the disease occurs in the postulated cause, that when the postulated cause is removed the disease goes away and then when it's reinstituted it comes back.

Q. And you're not testifying the only way to fulfill those postulates is by animal studies, are you?

A. I think that it may not be the only way but it may be the only practicable way, because within the system that we are talking about, which is much more complex than a single bacteria, we have numerous

chemical factors that need to be identified and tested, and none of this, I think, is beyond the realm of being doable but it's certainly beyond the realm of doing it without vigorous financial support from interested parties.

Q. Are you of the opinion, Dr. Benditt, that the replication in animal studies of a particular hypothesis and its results is the only way to prove scientific cause?

A. That's a difficult question. I think currently my short answer would be yes. I'd be willing to entertain, you know, research proposals that try to address the subject differently. I could envision that it might be possible to do it in other ways but I think it would be very, very difficult.

Q. Okay. Are you familiar with what the attorney general's definition of cause is?

A. No, I'm not.

Q. Did you attempt to determine that from your review of the surgeon general's report?

MR. BORMAN: Excuse me. You first said, I believe, the "attorney general."

MS. FLYNN PETERSON: I'm sorry, surgeon general. I stand corrected.

A. Surgeon general. I believe I have read that but

I might have my memory refreshed.
Q. And as you sit here today, do you have any understanding at all with respect to what the surgeon general's definition of cause is?
A. I have an impression but I can't say that it's accurate without reviewing the materials once again.
Q. What is your impression?
A. I think the surgeon general's reports, as I have read them, basically deal with issues of association, and those associations are repetitively stated in that report -- or those reports, because there is roughly 20 or 25 of them, I'm not sure. And over the course of time from the first report, which I believe is about 1964, through the last one which I reviewed, which was 1989, the associations have been repeatedly stated and periodically the term "cause" drops in because of strong, presumptively strong associations. But nowhere in those reports, to my knowledge, is there scientific studies that actually demonstrate cause in a -- in an unequivocal sense. There is a lot of epidemiologic data.
Q. You state in your report on page 2 that your testimony in this case will focus on defining cardiovascular disease and we know that definition, as I understand it, is what you have set forth in

paragraph one; correct?

A. Paragraph one provides --

Q. Under the introduction.

A. Correct. Paragraph one provides a precieux, if you will, of my views on cardiovascular disease and is a rather concise statement but may not necessarily be everything I would ever want to say about it.

Q. And again, just focusing on definition?

A. Yes.

Q. There may be other things you would like to say about it. As you sit here today, do any of those such things come to mind?

A. No. We'll leave that for now.

Q. And then you say your testimony will focus on discussing the multitude of risk factors involved. Will you tell me what that is?

A. Well we were discussing the fact that in cardiovascular disease, there are many forms of cardiovascular disease but for the moment, just to focus on the issue, we will only deal with atherosclerotic vascular disease. In terms of atherosclerotic vascular disease, there have been many factors identified to be associated with development of atherosclerotic disease in populations. We group those predominantly into

modifiable and non-modifiable conditions. The non-modifiable ones I think we can dispense with relatively quickly, including genetic makeup, gender, things of that nature. The modifiable risk factors that have been identified in terms of coronary artery disease include hypertension, diabetes -- diabetes may or may not be entirely modifiable -- smoking, and lipid profiles, which also may or may not be entirely modifiable, and stress and about 200 other items or more. So I think that those are really what I'm referring to in terms of discussing that and we know that there are potentially synergistic interactions among risk factors and we know there are synergistic interactions among modifiable and non-modifiable risk factors, and in a given individual, then, when one talks about what caused the problem one needs to encompass all of these. And the reason that it's important for physicians is just not academic. I think this sometimes gets lost in the mix, but it's important for physicians to understand that it's -- that whereas risk factor A may be important, all these other risk factors need to be considered and in the treatment of the whole patient you must deal with at least as many of them as you can get your arms around. And we tend, by focusing on one risk factor

and say, well, that's the cause and the problem, to ignore the fact there are all these other issues that need to be considered in dealing properly with the health of that patient, and in short that's what I mean by "multitude of risk factors."

Q. And you noted there were some 200 risk factors?

A. Minimally speaking, yes. There may in fact -- I've heard of even more than that. Maybe some of these aren't important for us to concern ourselves about because they are minor, but nevertheless we again don't understand the potential synergistic interaction among risk factors. Things that might seem to be trivial when considered alone might not be so trivial when stacked up with diabetes or other risk factors.

Q. Are some of those risk factors more important to others -- than others?

A. Well at least in epidemiologic studies, we identify certain risk factors as being more important than others.

Q. What does that mean, in epidemiological studies?

A. Well epidemiological disease basically look at populations and they try to compare a population in terms of the incidence of disease and looks at that population to see what the elements of clinical

circumstances were for that patient. In other words, do they drink much alcohol, are they diabetic, are they women or men, et cetera, and then make some statistical analysis to say that the disease occurs more frequently in the population with one or other or more of these factors. And at that stage that's still okay. There is nothing wrong with that because that identifies potentially modifiable habits in that population.

It's important for physicians because that educates physicians and helps them educate their patients about what are modifiable habits that potentially could be beneficial to that particular individual's health. So that's all good. But when it comes to saying that because this risk factor is prevalent in this population; therefore, it was the cause of the disease, goes beyond where the science ends. It becomes now a public relations or public education statement that extends beyond what is, you know, really known.

Q. Doesn't it depend on how strong that epidemiological data is?

A. Well I think in the cause issue, I'd say that it may be very difficult in any epidemiologic data to have strong enough associations to establish cause.

I think what epidemiologic studies do is they weed out a lot of things maybe we ought not be wasting our time looking at so that, for example -- well, that would have been a bad example, ultraviolet rays. For example, we can't rule out ultraviolet rays but we can assume control populations and disease populations are exposed comparably to ultraviolet rays, so we don't need to waste a lot of resources studying ultraviolet rays on heart disease but we can focus on things like diet, we can look at stress, we can look at smoking, hypertension -- things that are associated.

In the history of coronary artery disease there is at least one skeptical paper, and I thought was kind of cogent, points out that a risk factor of 1.7 is rather low compared to the epidemiologic associations in terms of coronary -- in terms of, say, certain risk factors such as hypertension with stroke, which has a very high correlative value or risk value, far in excess of 4 or 5, so that when we are talking about what is a strong risk factor versus others, we, as was -- you pointed out in the American Heart Association meeting, they talk about major, in terms of heart disease, smoking and coronary artery disease had a risk factor of 1.7 versus hypertension

and stroke, which is orders of magnitude, or at least in an order of magnitude higher.

Q. Do you know what the risk factor is for smoking and stroke?

A. I don't offhand but it's certainly not as high as hypertension and stroke.

Q. Do you know what it is when hypertension is combined with cigarette smoking?

A. There is a synergistic relationship there and there is, as I pointed out, there are probably synergistic factors or effects among many of these risk factors.

Q. Is the one study that you noted just recently in your response to the last question, is that one of the ones that you have cited in your references?

A. Frankly, I don't recall. I've read so much material, I'm not sure whether it's in here or not. Yeah, I think it's actually reference 26.

Q. All right.

A. But that information that I just cited is published in a number of different places so I don't think it's -- it resides solely in that reference.

It just occurred to me, when we get into discussing the relationships of risk factors to disease, you said if the risk factor is extremely

strong and my response, as I recollect, is something to the effect I don't think you can take epidemiological data of any strength and make it causal without the intermediate steps of scientific experiments we talked about earlier, and that in the case of smoking and coronary artery disease, using as a gold standard hypertension and stroke, the risk factor for smoking and coronary artery disease is much, much, much less in terms of strength.

Q. As compared to?

A. I used as my gold standard hypertension and stroke. I'm not trying to belittle the risk factor of smoking to heart disease. I'm just trying to say in the context that you placed it, a very strong risk factor, I think we would say that it's not if we use my gold standard as the -- as the plateau.

Q. Your opinion also, if you continue on page 2, you note that in your testimony at trial you will address the complexities of interaction that occur between various risk factors for cardiovascular disease. What will you be testifying with respect to that?

A. Well I think this gets to the issue of synergies among risk factors. We know that certainly when you get, for example, in the -- in the case of stroke we

know that there are a number of synergies that occur among risk factors, for example the diabetic. A hypertensive diabetic woman at a certain age is at much, much higher risk. So whenever you have risk factors, you also have to wonder whether, if you take risk factor A and risk factor B, is the complete risk the sum of the two or is there some multiple effect, and at least in some disease states we think there is multiple effect among risk factors. The one that most comes to mind is thrombotic stroke, and where there has clearly been shown by epidemiologic study a synergistic, almost multiplying effect of several of the risk factors, particularly hypertension, diabetes, female gender and age. So that's -- that would be an example of the kind of thing that I think needs to be considered in addressing any risk-factor analysis.

Q. When you talk about the synergy of risk factors, is it true that certain risk factors, when combined, increase the risk of disease?

A. That appears to be the case, yes. That's my point.

Q. But in those cases, each might be an independent risk factor; correct?

A. Yes. And as we pointed out earlier, several of

the risk factors we have discussed are known to be independent risk factors.

Q. That would include cigarette smoking?

A. That's correct.

Q. You also indicate that you are going to testify regarding the uniqueness of each individual patient in regard to risk factors. Tell us what you mean by that.

A. Well I alluded to that earlier. I think in the care of patients, each individual patient brings to the table a whole set of different problems and so their family history, their stress environment, their personal habits, as well as any underlying associated diseases they might have, all contribute to the picture that we have of that individual, and the strategy of dealing with their illness or preventing, as we try to do, the illnesses has to reasonably reflect all of those things.

Now we can try to identify as many as we want or as many as we are capable of. We may not necessarily be able to modify a lot of them, and of course much remains up to the patient in terms of their compliance with your recommendations. Nevertheless, that's sort of the general picture of what I was getting at.

Q. Does the fact there are these unique qualities to each individual mean we cannot draw conclusions with respect to the population as a whole?
A. No. I think we have drawn important conclusions with respect to the population as a whole from the epidemiologic studies. We know about certain habits we think would be helpful if people modified, and I think that those are drawn from epidemiologic studies. There are certain extensions of that information that we perhaps go out on a limb with because part of our job is educating and taking guesses, if you will, at what future research might show, but if you asked is that guesswork or is that science, I'd have to say frankly that's guesswork based on some judgment that -- but not based upon data. So we have learned a lot, we have made some important -- we have established some important guidelines or education points.
Q. Do you believe epidemiologically drawn conclusions are always guesswork?
A. No, I wasn't trying to imply that. I think epidemiologically drawn conclusions, based on good epidemiologic studies, which has its own science and own methodology inherent to it, that those are conclusions that are based upon valid observations.

The -- The usefulness of that relates to two issues I focused on. One is, it helps to weed out what we should reasonably focus on in terms of going the next step, which the next step in that realm would be to learn more about how a certain risk factor causes disease, if it does, or aggravates underlying disease, if it does; and two, how to best go about treating that problem or preventing it. And then on the other side of the coin is the more softer one, which is the taking the guesswork, the next step and saying, well, this appears to be the trend, let's make some educational statements and hopefully give the population a heads up, if you will, as to what we think we are going to learn if we pursue that first set of problems to their ultimate conclusion.

Q. Do you have an opinion as to whether if additional animal studies were done they would more probably than not establish the epidemiological conclusions that have been reached with respect to the relationship between smoking and cardiovascular disease?

A. That's a difficult question because there are two ways to approach it. One is sort of a gut feeling of personal opinion, which isn't worth a whole lot, but I can say that I think if you pursued

the scientific studies that would be necessary that ultimately you would find there was some relationship, causal relationship between a number of risk factors, possibly even including smoking and the disease process. That's sort of a personal gut feeling. Based upon my review of what's been done in the science so far, it appears as though the methodology for those experiments has not been derived yet because the experiments so far that have examined that, particularly inhalation animal experiments in animals, have yet to -- to be positive, and that may reflect just the fact we don't have the right models or it may reflect the fact that I'm wrong in my personal opinion.

Q. But, doctor, my question was: Assuming those methodologies could be developed, do you have an opinion as to whether it's more probable than not that those studies would support the conclusions reached on epidemiological data? Again referring to cigarette smoking and the development of cardiovascular disease.

A. I think ultimately we can demonstrate the epidemiologic data is accurate in animal models. I don't know that we can necessarily say that one single risk factor can be ultimately proven to be the

-- to be all of the problem. It may well be that these risk factors are independent, that we need to identify whether there is interaction among risk factors that we haven't even considered or have a knowledge base for identifying. I'm not trying to quibble with you; I just don't want to give up a scientifically valid approach. Because if I walk into a set of experiments and say my job is to prove that X causes Y, that's really not a scientifically appropriate way to approach a problem. My job is to provide a hypothesis and then go about developing methodologies that would identify whether that hypothesis is valid.

Excuse me a second.

(Discussion off the record.)

Q. Do you understand the difference between legal cause and scientific cause?

A. No.

Q. What is your definition of scientific cause?

A. Well definition of "scientific cause" is basically that a factor that's identified leads to an outcome that is identified -- that is provable based upon some methodologies such as I described earlier with Koch's postulates and that other factors have been excluded from the mix so that there is a

hard-and-fast relationship between if you do this you will get that result. And it may well be that in a disease process that would appear to be the case epidemiologically may not prove to be true scientifically because of other confounding factors, which our knowledge, as hard as we are trying to learn about stuff, our knowledge is limited and we just don't have the way to eliminate the confounding factors.

Q. Doctor, have you ever -- do you understand -- Let me rephrase the question.

Do you understand that from a legal standpoint in the state of Minnesota that the cause, in the type of litigation we are involved in, is defined as a -- cause is defined as something that plays a substantial part in bringing about the harm. Have you ever been given that definition?

A. No, and that's certainly a legal definition that's outside of my area of expertise.

Q. And do you understand that in -- from a legal cause sense that there may be more than one direct cause of an injury?

MR. BORMAN: Objection, lack of foundation.

A. I guess I understand that in the sense that you have told it to me and it isn't -- it isn't

unreasonable.

Q. And in fact in the scientific context, there may be more than one cause of any particular disease; isn't that true?

A. I think that's true, yes.

Q. In fact, that's what we have been talking about all morning, is multiple risk factors.

I'd like to go forward in your opinion. In the last paragraph that appears on page 2, you indicate what the basis of your opinions in this litigation will be and your academic training and experience, which I assume has been accurately set forth in your curriculum vitae which for our purposes has been identified as Exhibit 3800. Is that correct?

A. Yes, I believe that's true.

Q. And further your clinical training and experience, which I assume is also set forth correctly in your curriculum vitae?

A. It is.

Q. And then the scientific literature. Is the scientific literature on which you base your opinions and testimony in this case, is that literature, other than those things we have already discussed, which I will include as information and references provided to you by the attorneys in this case and research

that you have done yourself in preparing for opinions, is it any other scientific literature?

A. Well it may be scientific literature that I come upon as part of my continuing study of the problem and that would be, in my estimation, literature that is peer reviewed and has sufficient scientific merit to be worth reading.

Q. So you intend to continue to research up until the time of your trial testimony?

A. Yes, I do.

Q. Now --

THE WITNESS: Can you excuse me just a moment? I'm sorry to interrupt, but these people are being disturbingly persistent.

Witness checks pager.)

(Recess taken from 11:31 to 11:39 a.m.)

BY MS. FLYNN PETERSON:

Q. Doctor, again, before you left, we were just talking about the various bases for your opinions and testimony in this case. The next item you note is expert reports, which I understand you have only been provided with an access to two reports, Dr. Graham and Dr. Samet. Is that correct?

A. To this date, that's correct.

Q. Have you requested any other reports?

A. I have not specifically, but if I'm provided them, I'll use them.

Q. You also note deposition testimony concerning this case. Have you been provided with access to any deposition testimony, either directly or indirectly?

A. I haven't reviewed any depositions to this point but if provided them, I would use them.

Q. Has anyone summarized for you, either in writing or verbally, the testimony of any witness in this case?

A. No. My only recollection is that it was mentioned that a deposition of Dr. Graham was taken, but I don't know anything more about its substance.

Q. You note that a bases may be documents produced by plaintiffs. Have you seen any documents produced by plaintiffs?

A. The documents that I have, I have. I don't know who produced them, whether they came from the plaintiffs or from others, so I may have.

Q. Are those documents anything other than medical literature to this time?

A. Essentially the medical literature.

Q. Do you have anything other than medical literature?

A. The expert testimony reports of Drs. Graham and

Samet, and I think we mentioned earlier that I had at least reviewed the -- what I call the complaint, and you used a different term.

Q. Okay. I think the complaint was the term I used, but you had described what I believed to be a complaint.

A. Okay.

Q. Now you say you have the reports of Dr. Samet and Dr. Graham?

A. I have reviewed them. I do not -- I do not have them in my possession.

Q. So there are no other documents, then, when you say "documents produced by plaintiffs," other than those you have just described for us?

A. To my knowledge, there are no others that I would rely on. I would use whatever was provided to me or I found subsequently, if it seemed pertinent to the issue.

Q. Have you reviewed any medical records?

A. Not to this point I have not.

Q. Has anyone told you what has been in anyone's medical records in this case?

A. If I may just clarify, I've reviewed many, many medical records but no medical records pertinent directly to this. That's what you were referring to,

I think.

Q. I told you at the beginning what we are doing is reviewing that portion of your report that indicates the basis for your opinions and testimony in this case. So you can assume, for the purposes of my questions I'm asking, that's what we are referring to.

A. Okay. The reason I wanted that clarification is, because obviously in the course of my day-to-day activities I review many medical records and those medical records may not be materials that are directly pertinent to the case but have a direct relationship to my opinions regarding risk factors in vascular disease, and so in that regard I think that medical records that I've seen may be relevant but I haven't reviewed any specific -- I haven't been asked to review specific medical records directly related to issues here.

Q. Have you --

Has anyone provided you information regarding the data that is included in the medical records of the Minnesota Medicaid recipients in this case?

A. I have in verbal discussions been given some information regarding the acquisition of information that was apparently accessible in regard to those

individuals, and it's upon that information that I based some statements in here but I have not been the primary source myself of acquiring that information.

Q. What information have you been told in these verbal discussions?

A. My understanding is that it fits with my personal experience that the Medicaid population represents a socially deprived population that has the benefit of state-provided medical care in many instances and that the data, as well as my experience, would suggest that this population has a multitude of other risk factors in association -- or in conjunction with any given risk factors such as smoking, and that would then fit with the concept that trying to ascertain a specific percentage of risk for a given risk factor might be exceedingly difficult.

Q. What do you mean, socially deprived?

A. Individuals who may have lower income levels, or no income, or income that's derived from grants or welfare from the state or the county or who, due to disabilities, may not be in an income-producing position and have to rely upon income derived from the state or county. I think that probably covers it.

Q. Do you recall what specific information you were given during the verbal discussions that led you to the conclusion these people were socially deprived?

A. No.

Q. Who gave you this information?

A. In discussions with various attorneys, it was noted to me that the Medicaid population was specifically one of the populations that was being discussed in this case, presumably because the state was providing medical care for the recipients of Medicaid, and that was my interpretation. The Medicaid population to physicians in practice in hospitals is part of our overall care population. We care for them just as we care for individuals who have privately paid, high-priced insurance. From a physician's perspective, there is no difference in how those patients are cared for, and there may be differences in what they are eligible for based on what's in the package, but that's out of our control.

Nevertheless, it's clear that from both our experience, from literature, and as I think will be ascertained if I reviewed these cases individually, that there are multiple risk factors associated with these populations that may be complicating our

interpretation of which risk factors cause or is associated with or the principal -- principally responsible for, however you want to put it, a given outcome.

Q. But you have not -- you don't recall what you were told specifically relative to the Medicaid recipients in this case?

A. To my knowledge I'm only told that, one, they are a party or at least the state is a party to the case because of the interest in the Medicaid population, and that seemed intuitively obvious to me; and two, this population appears to have multiple risk factors for disease, and that is consistent with observations and experiences of mine as well as published literature on the subject. Given the opportunity to review individual cases, i.e. the primary sources, I think I would be surprised if I didn't come to the same conclusions.

Q. Have you asked to review medical records of Medicaid recipients?

A. No, I have not.

Q. Have you reviewed any of the deposition testimony of the Medicaid patients who were deposed in this case?

A. No, I haven't read any of the depositions of any

of the patients.

Q. Were you asked to review those depositions?

A. No, I was not asked to.

Q. Did anyone summarize or tell you about any of the testimony that was given by those Medicaid recipients in this particular case?

A. No.

Q. You state in your report these individuals, Medicaid recipients, were "chosen to be representative of the Minnesota Medicaid population." What is your knowledge about how they were chosen?

A. My understanding was that this was a court-defined process. I know nothing more about it than that. I think that if one was not limited by some court restrictions to how many such patients' medical records one could review, then the data would perhaps be more comprehensive; but given my understanding of the limitations, there is only a certain set of data that will be allowed to be examined. So in the sense that -- that it's arbitrarily established, all we can say is it is likely to be a -- or at least the best we have is a representative sample.

Q. So you're not of the opinion that the sample

here is representative but just that it's a sample you ended up working with; is that what your testimony is?

A. I can't say whether it's representative or not because I don't have access to know what the population looks like. All I can say is we were given an arbitrary sampling of the population. I'm not a statistician. I would be very interested to know whether a statistician thought this was anywhere like a reasonable estimate of what the population looked like. Nevertheless, that's what we are stuck with.

MS. FLYNN PETERSON: Would this be a good time to break? I'm going to go into a different area now that we have completed the basis of his report. I have just a few minutes before 12.

MR. BORMAN: That would be fine with me. Doctor?

THE WITNESS: Sure.

(Luncheon recess taken at approximately 11:50 p.m.)

A F T E R N O O N S E S S I O N

(Deposition reconvened at approximately 1:17 p.m.)

BY MS. FLYNN PETERSON:

Q. Dr. Benditt, we were going through your report. I'd like to continue that process as we start here again after lunch. If you could look at page 4, please, and I believe some of these concepts we may have covered even though we have not dealt with this part of the report specifically, but let's go through them.

You have defined "risk factor" here as "consistent association of identifiable characteristics noted in apparently healthy individuals that is thought to be related to the subsequent development of disease." Did you get that definition from somewhere or was that your own definition?

A. I think that's just one that was adapted from a number of sources but probably reflects my own view of it. I don't recall a specific citation or else it would have been provided there.

Q. And again with the specific disease entities we are concerned with with your report, cardiovascular disease, which you included coronary heart disease,

cerebral heart disease and peripheral vascular disease, you indicate that is a multifactorial and complex process. What do you mean by "multifactorial and complex process"?

A. The term "multifactorial" just means there is a number of factors which participate in either causing or exacerbating the problem, and "complex" implies that there may be interactions among these many factors and probably including interactions that we don't understand currently.

Q. And the "multifactorial," then, would refer to the various risk factors that you go on to explain in the next sentence?

A. Yes. I think the principal implication is that there are many, many risk factors, many more perhaps than -- than we currently understand.

Q. After the next sentence, "Over 200 different risk factors for cardiovascular disease have been identified in published medical and scientific literature," you cite reference number 1, and that is an article, the editors are Hopkins and Williams. Are you familiar with that article?

A. Uh-huh -- Yes.

Q. Let me ask you, how did you go about selecting these references?

A. These were just generally easily available and accessible references. Many of them are fairly classic. By "classic" I mean if you went to look for them or if you discussed this issue, people would continually, repetitively come up with them. For example, reference number 2, reference number 3 and reference number 4 are all what I would consider to be classic things. There are some others here that would similarly qualify.

Q. In seeking the references that you have cited in support of your report, did you attempt to cite those references that were reasonably reliable authorities in the area of cardiovascular medicine?

A. Yes. I thought that we cited references that are from largely peer-review journals or from very well-established textbooks, and that as a rule one could assume that the teachings in those are reliable. I wouldn't say that every word in them is, you know, gospel, but certainly as a rule they are reliable sources to obtain teachings regarding this subject.

Q. With respect to that first reference, the one that is -- I have a copy of it, is Atherosclerosis. Is that a journal?

A. Yes.

Q. And that particular reference is, as the title states, "A survey of 246 suggested coronary risk factors"?

A. Correct.

Q. Doctor, in the article that you cite there is Table 1, which are coronary heart disease risk factors and suggested associations. This appears to be a multipage table where it looks like the 246 risk factors might be listed.

A. They appear to be listed there, yes.

Q. Okay. I note that the article says that some factors in Table 1, such as cigarette smoking and, more recently, high blood pressure, are accepted by most experts to be causally -- excuse me -- to be causal for CHD, coronary heart disease, because of the results from intervention trials. Do you agree with that?

A. Except for the term "causal." I think that in the con -- taken in this context, one could say that some people might accept that, not all people, and I don't think we necessarily have to accept that.

Q. Do you agree that causality can only be proven by intervention trials?

A. I think that "cause" in the scientific sense could be proven by an intervention trial with

withdrawal and then reintervention, so depending on how you want to define an intervention trial, we sort of went through that a little bit earlier this morning, but I think that if that -- if you define an intervention trial as being one that fulfills Koch's postulates, then that would be an acceptable trial.

There may be other models that would be acceptable. I can't think of one offhand but there may be other models that would be acceptable that would have to be discussed.

Q. Do you know what is meant in this article by "potentiators"?

A. I probably do, but I prefer to read the context in which it's seated.

Q. The article talks about a classification of risk factors: Initiator, potentiators and precipitators. Do you know what's meant by those terms?

MR. BORMAN: I guess I'm going to object unless you let him look at how those are used in the article. Will you allow him to look at the article?

MS. FLYNN PETERSON: He cited this as a reference and my question is simply if he knows what those terms mean in that article.

MR. BORMAN: Still, I think my objection is that he should have a chance to look at them in the

article. He may not recall.

MS. FLYNN PETERSON: If he doesn't recall, he can -- he can tell us that.

A. I would have to review the article in order to assure myself that I knew how they were using those terms. It's been a while since I've looked at them.

Q. So as you sit here today, you don't recall what the article -- how the article defines the terms of initiator, potentiators or precipitators; is that correct?

A. That's correct.

Q. Do you agree that cigarette smoking has been associated with increased platelet adherence and thrombotic tendency?

A. Yes, I -- I've heard that.

Q. Do you agree that the associated exposure to carbon monoxide from cigarette smoking may increase endothel -- endothelial permeability and precipitator arrhythmias?

A. It may do that.

Q. Do you agree that cigarette smoking qualifies as an initiator, promoter, a potentiator and precipitator of coronary heart disease?

A. It would again depend on how those terms were defined in that article, and if I could look at that

I probably would be able to give you a better impression.

Q. I believe all of those terms are defined, doctor, in the comprehensive classification of risk factor section of that article.

A. Okay. As long as we don't -- As long as we can keep referring back to this.

Q. And I've just remembered --

A. If I can remember it long enough.

Q. -- with those definitions in mind, would you agree that cigarette smoking qualifies as an initiator, a promoter, a potentiator and a precipitator of coronary heart disease?

MR. BORMAN: I'll object to the form of the question.

A. The way I would respond is that in the manner in which the authors have discussed cigarette smoking, and if I recall correctly they say it's a possible potentiator. I think I've quoted them correctly, at least on the pages that you showed me.

Q. Do you agree or disagree with that statement, then? Are you saying you disagree?

A. That it's a possible potentiator? I would agree with that.

Q. And again I would just ask you to refer

specifically to, and I think you can answer yes or no whether you agree or disagree so I'm sure of what you stated, cigarette smoking qualifies as an initiator, promoter, potentiator and precipitator of coronary heart disease, do you agree or disagree with that sentence?

MR. BORMAN: Same objection.

A. I disagree with that sentence. Is that a sentence that's quoted from there?

Q. Yes, it is. Do you agree or disagree with that sentence?

A. I disagree with that sentence.

Q. Your report further states that cigarette smoking is included among the major risk factors for cardiovascular; is that correct?

A. Yes, that's correct. Again the term "major" is a term that I would just as soon not be in there since I don't know what that means, but we have discussed that earlier.

Q. Was that your term, Dr. Benditt?

A. "Major"? I thought you just quoted. Didn't you just say that?

Q. I'm quoting your report, "Major risk factors."

A. Oh, no. That's a term that seems to be prevalent in the -- in the literature. Now that you

point it out, I probably would prefer not to have put that there.

Q. You indicate that in paragraph three, in the section on page 4 entitled risk factors, it is your opinion that risk factors do not constitute proved cause-and-effect relationships in regard to disease development. Is that still your opinion?

A. Yes, that's correct.

Q. And I note you have cited for that --

A. Dr. Levy's paper.

Q. Reference 2, which is Dr. Levy's paper, but that is included in a textbook Heart Disease; is that true?

A. That's correct.

Q. You have indicated that's one of the classic cardiovascular textbooks?

A. It is.

Q. Did you review the references you cited for your report in preparation for your deposition today?

A. Yes, I did.

Q. What other materials, if anything, did you review in preparation for your deposition today?

A. My expert testimony for -- I can't say I read it from cover to cover but I reviewed the surgeon general's reports from 1983 and 1989, reviewed the

article which you have in front of you by Levy and the one that you have discussed just -- I did not look at the Atherosclerosis article, just recently, and about eight or ten other articles just to refresh my memory on the general aspects of the problem, several of which are cited in the references to the expert testimony.

Q. In Dr. Levy's article, do you agree that the overwhelming evidence supports a strong and definite relationship between cigarette smoking and coronary artery disease?

A. As you've quoted it there, yes.

Q. Do you agree with Dr. Levy that the most prospective disease with sufficient data tend to show the risk of developing coronary artery disease is directly related to the number of cigarettes smoked per day?

A. There appears to be evidence in that regard, yes.

Q. Do you agree with Dr. Levy that numerous investigations have demonstrated that cigarette smoking is also a major risk factor for myocardial infarction and death due to coronary artery disease?

A. Yes, it's a definite risk factor.

Q. Do you agree with Dr. Levy that cigarette

smoking has definitely been implicated as a major contributor to cardiovascular mortality and morbidity?

A. Yeah, I think the term "contributor" remains. Again, it's a factor that predisposes to risk of those things, yes.

Q. So individuals with coronary artery disease that smoke, there is a percentage of their disease that can be attributable to cigarette smoking, isn't there?

A. I think the answer to that is yes, but how you might make such an attribution is something that I think we would have very great difficulty with.

Q. Risk factors, in your opinion, show only associations; is that correct?

A. Risk factors are associations.

Q. And that an "association" you define as a statistical relationship that may or may not imply a causal relationship; correct?

A. That's correct, yes.

Q. And you cited that in reference 3?

A. And it's also cited in reference 2.

Q. In reference 3, did you review this reference in preparation for your deposition today?

A. I've not read that one for many months, but it's

brief.
Q. The article is on clinical epidemiology and it talks about this methodology I think you and I have been discussing --
A. Yes.
Q. -- this morning in a variety of different ways. There are -- There is a section on interpretation of an association, if I could just refer you to that. It appears that's the section of the article, is it not?
A. Yes, there is a section that's written that way.
Q. I'll show it to you in just a moment. Let me read it. With respect to risk factors and association, does this author state that: In the absence of evidence from clinical trials, observational studies can provide evidence supporting causative association between risk factors and disease?
A. He so states, yes.
Q. And do you agree with that or disagree with that?
A. I think the way it's written is accurate, yes.
Q. And this author that you have cited then goes on to indicate that causation can be strengthened if a

number of conditions are met. Do you see where I'm referring to?

A. Yes. He says the causation is strengthened under the following conditions, and it lists a number of conditions.

Q. And those include, the stronger the association, the more convincing is the evidence that the relationship is causal. Do you agree with that?

A. Yes.

Q. Do you agree, as the author states, that strong associations are less likely to be the result of uncontrolled confounding?

A. Yes. I think that this is correct. The caveat in each of these, I might as well just put up front, is that what is a strong association? They don't deal with that. And in the -- the real issue, then, isn't whether we agree or disagree with the statement. The statement is sort of like apple pie stuff. The issue of strong associations versus weak associations is the essence of the problem, and as I alluded to earlier this morning, if you use the gold standard, and you may not wish to do it, but if you use the gold standard, the relationship between hypertension and stroke, then the strength of the association between smoking and coronary artery

disease is a relatively weak one. And I don't mean to down play the association as being unimportant. I'm trying to characterize the concept of strength and association, which to my knowledge they don't discuss here. It's done rather qualitatively.

Q. And in this article that you have cited as one of the references to your opinion, did you attempt to determine through any other articles how to define strength of association?

A. Actually I did, and I would refer you to reference 26. I believe that's the correct reference, reference 26 in my expert testimony, that -- that basically addresses this very same issue that I just gave you, but they -- but they have got the real numbers. I was close, I think, but their statements are much more precise than mine.

Q. Would you agree, Dr. Benditt, that the likelihood that causation is strengthened under the following conditions would be the stronger the association, the more convincing is the evidence that the relationship is causal? Do you agree with that statement?

A. Yeah. Well evidence is more convincing, but establishing scientific proof is an element of having lots and lots of evidence that is based on reasonable

scientific study --

Q. Would you --

A. -- so --

Q. -- agree that causation would be strengthened if studies demonstrated exposure to the risk factor antedates the onset of disease?

A. It would be convincing under those circumstances, assuming that control group didn't evidence onset of the disease in the absence of exposure to the risk factor.

Q. Would you agree that causation would be strengthened if the association is shown to be dose dependent?

A. Yes, I think dose dependence is a valuable observation, but again one needs to demonstrate absence of the disease in the absence of the risk factor.

Q. Well if you have a situation, would you agree that somebody who smokes two packs of cigarettes a day has a higher statistical incidence of myocardial infarction than somebody who smokes one pack of cigarettes per day?

MR. BORMAN: I'll object to the form of the question.

A. There appears to be evidence to support that

contention. The elements that need to be clarified, though, and I'm not sure that we can do that here, are whether there are other factors that go on in the lives of those people that play a role, one that's been raised in the literature, and there is a citation on psychosocial aspects of smoking and I think it's cited here but I'll have to pull it out.

Q. I believe it is.

A. That deals with the issue of why do people smoke two packs of cigarettes per day rather than two cigarettes per day, and it may relate to many other factors in their lives such as stress, other personal habits and what have you, and I'm not trying to pooh-pooh the notion that there is a risk-factor relationship. I just think we need to in this discussion look at it very critically and say is the dose-response relationship a pure one or could it be affected by other confounding variables that we can't necessarily put our arms around in a population study. So with that caveat in mind, that's where the -- that's how we have to interpret the dose-response issue that you just raised.

Q. And just because someone who experiences coronary artery disease or coronary vascular disease, if they are a smoker and have other risk factors,

that doesn't mean the smoking isn't an important cause of that disease, does it?

MR. BORMAN: Objection to form.

A. It doesn't mean that it isn't an important cause, it doesn't mean that it is. It means that there are multiple factors in this patient that have precipitated the disease and there may be other factors that may have potentiated the disease and determining which is which, and what relative magnitudes of influence they play is a very daunting task.

Q. Would you agree, Dr. Benditt, with the studies that have been done to date that there is overwhelming evidence that cigarette smoking plays a substantial part in the cause of coronary artery and coronary vascular disease?

A. Well to the extent that you define the risk factor of 1.7 as substantial, then the answer would be yes, but I think that we again have to establish what "substantial" means in the risk-factor world. And we know that there are risk factors to disease that are sometimes, you know, four or five or even many fold more than 1.7, so I'm -- depending on a judgment here as to what "substantial" means, it's a rather qualitative term.

Q. What do you mean by risk factor of 1.7?
A. That means that there is -- I think that's the standard number, incidentally, that's commonly in literature. You probably have seen 1.68, 1.7. It represents a -- if a population had no increased risk of a given disease, or I should put it if a factor resulted or was not associated with an increased risk of disease, then it would be 1.0. In other words, the disease in the population is uninfluenced by that factor. If the disease in a population is influenced to the extent of 1.7, it means that 1.7 times what you would expect the disease in that population to be. It's commonly said, and perhaps epidemiologists would argue with me and I'd have to defer in that regard, but commonly said that a risk -- that 3 is a lot.
Q. Is what?
A. Is a high number. And the citation for that actually is reference 26. The -- That -- I'm not -- You know, I think it's probably an arbitrary number, and I'm not trying to pooh-pooh 1.7 as being negligible. That's not why I'm here. But in terms of what is substantial or major or whatever, we don't have -- we don't have a number that qualifies as substantial or major.

Q. Do you agree that when we are discussing risk factors and associations that the likelihood of causation is strengthened if the relationship is consistently demonstrated under diverse circumstances either in various populations or using different measurement methodologies?

A. I think that comes from the Furberg, I think that makes some sense, recognizing that all of those kind of studies would be inferential and indirect.

Q. Would you agree that, again we are discussing risk factors and their associations, that the likelihood of causation is strengthened if the association is biologically plausible?

A. Yes, I think it would have to be biologically plausible.

Q. And would you agree that the likelihood of causation is strengthened if the association is specific; that is, the risk factor is associated with a particular disease?

A. That's a different way, the use of the term "specific," than we are accustomed to using. Generally one would expect that the absence of that risk factor in a normal population would be unassociated with the disease. I guess the way I would look at it is a qualified yes to that. I think

the term, the way they use the term "specific" is different than the term "specificity."

Q. And they define it as, again, it says the association is specific; that is, I'm assuming definition, the risk factor is associated with a particular disease.

A. Well that increases the strength but they also have to consider what other factors might have been present at the time. I mean, that has to be a given in conjunction with item 6.

Q. Would you agree, if you took all those six factors we just discussed, that the likelihood of causation would be strengthened if the study met all of those six factors?

A. Yes, if the study meets all six factors.

Q. Would that, in your opinion, lead to causation?

A. Not necessarily. I think it strengthens one's concern, and I think this is the importance of the epidemiologic process that they are alluding to in that ultimately we would like to learn of causes and therefore -- or thereby improve our ability to prevent and treat and the epidemiologic process helps to weed out things that are potential contributors and get our -- and get us focused on the more important types.

Q. As we continue to discuss your opinion, you indicate that a risk factor is not considered causal based only on statistical valid epidemiological associations. Is that still your opinion?

A. Yes, that's correct.

Q. And again as I understand it, you would not agree that interventional studies can lead to determination of cause.

A. There are too many negatives in there. Can you state that more simply?

Q. Would you agree cause can be proven by interventional studies?

A. Yes, I think cause can be proven by appropriately designed interventional studies.

Q. Has cigarette smoking been identified as one of the significant risk factors in the development of coronary artery disease?

A. Yes. The term "significant" is another qualitative term but I think we would not quibble with that.

Q. Doctor, one of the references you cited, number 7, I believe is one of the ones you were referring to earlier. It talks about the social and psychophysiological factors in coronary heart disease.

A. Okay.
Q. In that article, when they are talking about the pathophysiology of cardiovascular disease in humans, the authors state, cigarette smoking is another risk factor with definite physiologic consequences resulting from nicotine and carbon monoxide exposure. Do you agree with that statement?
A. Yes, as you've quoted it.
Q. You were following along. Did I read it correctly?
A. No, I think you did read it correctly.
Q. When we discuss cerebrovascular disease, in your opinion, would you agree that smoking seems to be an independent risk factor for acute brain infarction?
A. Yes, smoking seems to be an independent risk factor in conjunction with cerebral disease of the atherosclerotic type.
Q. And you contrast that atherosclerotic type from cerebrovascular disease related to thrombus?
A. I'm particularly concerned about cerebrovascular disease related to vascular spasm, embolic events which may have other etiologies. I think those are the principle ones, plus the implication of hypertension, which is the most powerful known risk factor to brain infarction.

Q. Did you review the article by Dr. Hart and Dr. Solomon that you referenced in number 15 of your references?

A. If it's in the references, I reviewed it. I can't say I reviewed it in the last few weeks, though. This one I have not reviewed in the last many months.

Q. Would you agree with these physicians that cigarette smoking is an established risk factor for cerebrovascular disease?

A. Yes.

Q. Do you agree that reduction in smoking can lead to the decreased incidence of stroke in the population?

A. Yes, I believe I would.

Q. In your report you state that "Although smoking has been identified as a risk factor for cerebrovascular disease, the consistency of data relating cigarette smoking to cerebrovascular disease, including stroke, has been questioned." What do you mean by that?

A. Well certainly the most powerful risk factor is, to my knowledge, hypertension. The literature on the relationship of smoking to stroke is also infiltrated by other confounding risk factors in that population,

including hypertension in women -- well, hypertension, gender, diabetes in women and oral contraceptives and other medications, so I think that there is some variability in the outcomes of the studies. Nevertheless, we recognize smoking to be a risk factor to the vascular system.

Q. Are you aware of any studies or papers that have concluded that cigarette smoking is not related to the development of cerebrovascular disease?

A. That's a question that I actually was aware of a paper, and I don't know whether I have the citation for that. And I think the vast majority of the risk -- of the literature would cite it as a risk factor.

Q. Reference 18 is an article from Stroke, which is a publication, peer-review publication, is it not, Dr. Benditt?

A. Yes, it is.

Q. And it also is a publication supported by the American Heart Association?

A. That's correct.

Q. Table 2 of reference 18 is entitled Summary Statistics for Significant Risk Factors in Stroke Profiles. Do you see that?

A. Yes, I do.

Q. It lists, among other risk factors, cigarette smoking?

A. Yes, it does.

Q. Would you agree that cigarette smoking is a significant risk factor in stroke profiles?

A. I'm just going to take a moment to review what these numbers are on this table.

It appears that this table lists, in percentage terms, the relative numbers of patients with strokes that were -- that exhibited these risk factors.

Q. Uh-huh.

A. That appears to be what the table shows.

Q. And the table is entitled Summary of Significant Risk Factors in a Stroke Profile?

A. That's correct, but it doesn't -- the table doesn't, as I first thought when I looked at it, provide a statement regarding the relative power or strength of the risk factor. It simply says in such a percentage of the population these observations were found. That's my understanding of this table.

Q. And my question was: Would you agree that cigarette smoking is a significant risk factor in stroke profiles?

A. Well it's listed here as being present in a third of the patient population who had stroke. What

I don't know is in the control population which percent -- what percent of men and women in the population who hadn't had strokes smoked. That's not provided in that table. I think there is another table in that paper that's maybe -- that deals with the relative risk scores.

Q. I think you are looking -- are referring to Table 4, aren't you, which talks about the ten-year probability for stroke according to age of men and women?

A. Yes. Actually I was looking at Table 3, --

Q. Okay.

A. -- I think, where it talks of -- it gives relative risk in men and women for each of these risk factors. And one notes, for example, that cigarette smoking is listed again, in this case at 1.67, is very similar to that 1.7 number we were talking about earlier, 1.67 in men and 1.7 in women versus an elevated systolic blood pressure. If we look at that it's 1.9 in men and 1.7 in women. Atrial fibrillation, which is a renowned risk factor, speaking of strong risk factors, is 1.8 in men but over 3 in women, is one of our most important medical concerns these days, and you notice that left-ventricle hypertrophy is comparable in men and

women, over 2, which may in fact reflect hypertension. Sometimes hypertension gets burned out and all you see left over is left-ventricle hypertrophy.

Q. Based on those statistical correlations, do you agree with the authors of this study that cigarette smoking is a significant risk factor in a stroke profile?

A. Yeah. I think they know that it's statistically significant and that they have given you a number upon which to compare smoking to other important risk factors, which is the value of that paper.

Q. You have also cited as reference number 19 a study regarding risk factors for various manifestations of cardiovascular disease which was based on 30 years of follow-up in the Framingham study. Do you recall that article?

A. Yes. This also falls under what we call as classical articles of cardiology.

Q. Would you agree with the authors of that article that the contribution of cigarette smoking is strong and consistent across various manifestations of cardiovascular disease with exceptions perhaps of TIA and CHF in women?

A. Yes, there is a consistent association, as they

point out.

Q. Do you agree with these authors that cigarette smoking may act as both a thrombogenic and arrhythmic trigger; however, the fact that it is a most important risk factor for intermittent claudication suggests it plays a part in atherogenesis?

A. The first part I think is a reasonable statement. The last part, I'm not quite sure how they made that connection, because certainly we know that a number of the chemicals in or at least believed to be in cigarette smoke may cause narrowing of the -- functional narrowing, and that could happen in the heart as well as the periphery. I don't think one needs to necessarily leap to claiming that it's a cause of atherosclerosis. It may or may not be. But what they point out there doesn't have to make that inference.

Q. So you don't agree with the authors with respect to the second part of that sentence?

A. Correct.

Q. Reference 20 from the Journal of cardiovascular Pharmacology talks about the epidemiology of peripheral artery disease, and I would ask you whether you agree, in that study that you have cited, with the authors that the risk factors associated

with the incidence of peripheral vascular disease are indisputably age, smoking and hypertension.

A. Those are the most important ones, although I think they omitted one other, which is genetic predisposition.

Q. More likely in women or men?

A. Can't answer that. I know that it's got to be strong in men. I don't know that it would be any different in women.

Q. You indicate in your report that there have not been uniform findings of any relationship between smoking and stroke. What did you base that opinion on, Dr. Benditt?

A. Can you point out where --

Q. Sure. We are in paragraph 4, page 6.

A. Well it looks like I cited the U.S. Department of Health and Human Services publication, and I know that also in reference 26 there is a discussion of the paradox that relates or shows not a tight relationship between smoking and stroke, probably because of the very high importance associated with hypertension and atrial fibrillation that I alluded to earlier.

Q. Okay.

A. And that may mask some of the lesser risk

factors.
Q. So you base that conclusion on the Department of Health and Human Services report, reference 25?
A. Yes, plus I'd also, although not cited at the specific spot in here, reference 26.
Q. Twenty-six as well, okay.
You agree that cigarette smoking has been statistically associated with intermittent claudication?
A. Yes.
Q. You have a portion of your report where you discuss the biological mechanism by which smoking may contribute to the development of cardiovascular disease and you conclude that that mechanism is not known.
A. Could you just show me which part you're looking at?
Q. Page 7. Do you see the portion of your report that's the last section on page 7?
A. Yes, I have it.
Q. I don't see any references cited for that particular portion and I would ask you, Dr. Benditt, what you are relying on to make the conclusion that the biological mechanism by which smoking may contribute to the development of cardiovascular

disease is not known?

A. Well I think we could probably refer to virtually any of the standard textbooks under the pathogenesis of atherosclerosis, Ross and Braunwald's heart disease. I think, if I remember correctly, we will find a number of statements regarding potential damage to endothelium that have no direct relationship between smoking and the development of heart disease.

Q. You said that you believe that you would see a number of statements regarding the potential damage to the endothelium. Tell me, can you explain for me what you understand those -- that relationship to be?

A. Well it's been purported, and probably there is some truth to the fact that chemicals that have been associated with smoking, including nicotine and carbon monoxide, damage endothelial layers in blood vessels. I think there is experimental evidence to suggest that, support that contention, uncertain as to whether, though, that ultimately results in atherosclerotic disease and it's also uncertain what relevance that would have versus, for example, the impact of those chemicals on people who would, say, develop atherosclerotic disease for other reasons, say one with hyperlipidemia who might already have

the disease in some manner or some magnitude, and whether the impact of these chemicals would exacerbate that or just perhaps cause some spasm of the vessel on top of that. These are issues that I don't think are known so it's difficult to -- I mean there is an association, no doubt, but what the cause-effect relationship is I think requires some more study.

Q. Has it been shown that for individuals with atherosclerosis that cigarette smoking aggravates that preexisting condition?

A. I think clinically there is evidence to that effect, yes, and certainly in advising patients who have no underlying heart disease, no previous heart attacks to peripheral vascular disease, we advise them to stop smoking, and the impression is that that's an important piece of advice. Does that prevent the continuation of the disease or future heart attacks? Maybe in a population study it would, but in an individual patient you can never really know.

Q. What about with respect to hypertension? You have indicated to us today that hypertension, in your opinion, is the major risk for stroke.

A. Yes.

Q. Does -- Does cigarette smoking for an individual with hypertension increase that risk of stroke?

A. I can't answer that question.

Incidentally, just to back up one spot, hypertension I think globally is perhaps the most important risk for stroke, but as we pointed out, atrial fibrillation may even rate higher numerically.

Q. Particularly for women?

A. Especially for women, yeah. But ignoring atrial fibrillation for the moment, because I don't think you are particularly interested in that, hypertension is certainly very important and the -- my knowledge, I just don't know whether there is a synergistic relationship between hypertension and smoking. I think that there probably is, but I can't cite you a source for that.

Q. You indicate that further research is needed to identify the factors in cigarette smoke that may be responsible for cardiovascular effects. What is your understanding of what chemicals are in cigarette smoke?

A. Well certainly there are many that have been -- many chemicals that have been defined, but I think the only ones that have received a lot of attention in terms of potential impact are carbon monoxide,

which is going to have a net effect on reducing oxygen to any tissue, and nicotine. Certainly there are many other chemicals that I can't quote you here but I don't think any others have been studied to the extent of those two.

Q. Do you know how many chemicals are in a cigarette?

A. I don't offhand, but I venture to guess there is probably hundreds.

Q. What about do you know just from a numerical standpoint how many chemicals are in cigarette smoke?

A. I wouldn't venture a guess.

Q. I wanted to go through some of the aspects of the surgeon general's report that you have cited. I believe they are references 5 and 25, by your number. Five is the 1983 report of the surgeon general, and 25 appears to be the 1989 report.

Do you agree with the surgeon general's report that cigarette smoking is one of the three major independent coronary heart disease risk factors?

A. Well I'd say that I agree that it is a -- an independent risk factor. The term "major," I'll again put my standard objection to the use of that term, and why they just chose three I'm not quite sure. I think there are a number of independent risk

factors.

Q. Would you agree with the surgeon general's, and again I'm referring to the 1983 report, that cigarette smoke acts synergistically with other major risk factors to greatly increase the risk of CHD?

A. I think that's an opinion that's widely held and I think there is some reason to believe that that's likely to be true.

Q. Would you agree that cigarette smoking contributes both to the development of atherosclerotic lesions and the clinical manifestations of atherosclerotic vascular disease, including sudden death?

A. The second part of that sentence I think is highly likely to be true. The first part of that sentence I think was highly speculative in 1983 and I don't even think we know for a fact in 1997 to be the case.

Q. Would you agree that cigarette smoking is the most important risk factor for atherosclerotic peripheral vascular disease which usually involves the lower extremities?

A. It's the most important modifiable risk factor in all probability. I think the genetic predisposition may be a more important risk factor

overall.

Q. Would you agree that cigarette smoking acts to aggravate and accelerate the development of atherosclerosis in the aorta more than any other blood vessel?

A. I can't speak to that issue. I don't have any personal experience with the aorta.

Q. Would you agree that although the specific mechanism by which cigarette -- excuse me -- by which tobacco smoke affects atherosclerosis have --

(Interruption by the reporter.)

Q. Would you agree, doctor, that although the specific mechanisms by which tobacco smoke affects atherosclerosis has not been clearly delineated, that the effects of cigarette smoking on the atherosclerotic lesions that underlie cardiovascular disease seem well established?

A. Yeah, the second half of that sentence is probably true. I think I'd have to read the sentence to see whether the word was "effects" or "affects."

Q. It's one of each, that's why it's difficult. Look at 3.

A. Make sure we have this correctly transposed.

Q. A-F-F for the first one and E-F-F for the second one.

A. That's an important distinction, I think, because the first one is A-F-F and the -- consequently that's certainly true. We don't know the mechanisms by which it affects. And I guess the second half of that sentence would be more accurately stated to be that we know what the effects of cigarette smoking are in the clinical circumstances, patients who have atherosclerotic lesions, but I'm not sure that we know what the effects of cigarette smoking are on the lesions themselves and I -- I've not seen any papers that actually show me that the cigarette smoking enhances the lesions or absence of smoking diminishes the lesions.

Q. You disagree with that finding of the attorney general -- excuse me -- the surgeon general?

A. With the surgeon general. This is a 1983 report, and I think even in the 1989 report they point out that a lot of what was in the 1983 report was speculative.

Q. I understand that one of the distinctions you draw in this case with respect to cause is that the specific mechanism by which cigarette smoking may cause cardiovascular disease, in your opinion, is not known; is that correct?

A. Yeah, that's an important aspect of the opinion,

and the other element of the opinion is that we have many factors that play a role or appear to play a role and how they act together and to -- in what proportion one or all of them are blameable is beyond the resolution of our current knowledge.

Q. Would you agree that with respect to those risk factors that the most firmly established modifiable risk factors for atherosclerotic cerebrovascular disease are the hypolipidemia, hypertension and cigarette smoking?

A. Yes, that's certainly true. I'm trying to think of whether there might be others as well, and we might these days also include atrial fibrillation in there, although it's not so easily modified.

(Interruption by the reporter.)

Q. Doctor, would you agree with this conclusion of the surgeon general in 1983. I will read it and then I will give it to you to read because it may be difficult from this standpoint for us both to do the same thing. That the variety of possible pharmacological and toxicological implications of smoke and its constituents, in the absence of firm proof of what mechanisms are precisely involved, in the unequivocal cause-and-effect relationship between smoking and cardiovascular disease should not detract

from our confidence in the epidemiological and clinically irrefutable evidence of the cause-and-effect role of cigarette smoking in contributing importantly towards heart disease?

A. Well, I think it says for itself what it says. I --

Q. And I would just ask if you agree or disagree with that statement.

A. I would have to disagree with the statement. In 1983, they had -- I mean, this was much too premature to be published in 1983.

Q. Do you agree with it today?

A. I think even today that it's not supportable by scientific evidence. I think the epidemiologic aspect that they allude to, I'm not quibbling with that at all and it shouldn't -- we don't detract and I wouldn't detract from confidence from the epidemiologic associations.

Q. Is it the clinical portion you disagree with?

A. Yeah, this, quote, from clinically irrefutable evidence that the cause-and-effect role, unquote, that part I think is not supported. And as a matter of fact if you look in the 1989 report, the temporal -- they have this whole table of temporal developments which continues in 1989 to be

equivocal.

Q. One of the things that is -- that the 1989 report does is it goes through the different phases that have occurred in the surgeon general's report from 1964 through 1989. Do you remember that part of it?

A. Yes, I believe I do.

Q. And isn't it true, Dr. Benditt, that throughout those years from 1964 through 1989 that as successive reports were published and more evidence was available to the surgeon general, different conclusions were drawn with respect to the relationship between cigarette smoking and coronary heart disease?

MR. BORMAN: Object to the form.

A. My recollection is that they continued to modify their statements, becoming increasingly -- increasingly using new information. I don't think that there is to this day any hard-core data that would support that quotation that you had just read.

Q. Initially in 1967 the surgeon general reported that there was evidence to strongly suggest cigarette smoking could cause death from coronary heart disease. Do you recall that?

A. Yes.

Q. And it wasn't until 1984 that the surgeon general concluded that cigarette smoking was one of the three major independent causes of coronary heart disease; correct?

A. That's what he concluded in 1983.

Q. So there was an evolution of association from 1967 through 1983 relative to cigarette smoking and coronary heart disease; correct?

A. Well the 1967 quotation that I think you just gave us deals with the functional outcome of the impact of smoking in -- in patients with coronary artery disease. It doesn't say anything about cause-and-effect relationship because mortality or death can certainly occur in somebody who has underlying disease, is exacerbated by some risk factor. The 1983 report, at least the quotation that we were just discussing earlier, is much more dogmatic and I think is something that we would need to look for scientific evidence to support and I don't think exists.

Q. Would you agree that since 1964 the surgeon general has identified associations as causal between cigarette smoking and coronary heart disease, atherosclerotic peripheral vascular disease, lung and laryngeal cancer in women, oral and esophageal cancer

and chronic obstructive pulmonary disease?

A. Most of those topics are outside my area of expertise, but within my recollection of having looked at the report, that's my understanding of what they claim. I can't pretend to know the scientific basis of most of those claims unrelated to coronary artery disease so you will have to let me bypass all of those. I can only make a statement that says that no matter how they interpret the data, the scientific evidence doesn't permit us to be so concrete in terms of cause-and-effect relationship. Risk factors and associations that have -- is where they have developed that information from.

Q. Do you agree with statistics that in 1985 21 percent of the deaths related to coronary heart disease were attributable to smoking?

A. I don't have any -- I don't have any opinion on that. It may well be the case.

Q. What happens to somebody who is a smoker who quits smoking relative to coronary heart disease?

MR. BORMAN: I'll object to the question.

A. From an epidemiologic, you know, perspective, in a given individual, you can't predict but it's generally said that in a population-base study that the risk of manifestations of heart disease diminish

rather rapidly. They don't ever get back to base line, but probably within a year they are substantially reduced. And this doesn't necessarily mean, and in fact probably does not mean that the atheromatous disease has vanished. It probably more reflects the potential functional impact of smoking on top of an already preexisting condition. In other words, if you have a narrow vessel and take something that makes it narrower, you are going to have a problem. So I think that the -- we are not talking about reversal of disease. What we are talking about is diminution of the manifestations of a preexisting disease. I think that's why the statistics say what they say.

Q. What do the statistics say with respect to cardiac death?

MR. BORMAN: I'll object to that question.

A. I can't give you the exact numbers, but there is clearly a reduction of mortality risk associated with stopping smoking in patients with known cardiovascular disease at the time you have advised them to stop smoking, and that occurs relatively rapidly. I mean, it doesn't take 10 years to happen.

Q. Within the first year, doesn't it, Dr. Benditt?

A. It occurs very quickly, infers a functional

rather than a -- a functional impact, if you understand what I mean, as opposed to reversal of the disease.

Q. Tell me what you mean by "functional impact."

A. Well I suppose if one has a narrow blood vessel, say they have a disease and have a narrow blood vessel and I give you some medicine to -- that as one of its adverse effects narrows the blood vessel more, you might have gotten along quite fine with your narrow blood vessel but now all of a sudden I've narrowed it more. There are a number of medications that do that. We occasionally inadvertently do that as part of treating another condition, we end up aggravating something else. And I think that that then, if we stop that medication, we haven't created a new disease. All we have done is taken an existing disease and made it go from a tolerable to an intolerable situation, if you will. And if we reverse, take away that medication, we haven't eliminated the disease. All we have done is taken away the additional stress, if you will, on the system.

Q. Uh-huh.

A. Bad habits might be considered to be a very similar -- have a very similar impact. Certainly

smoking, since we are discussing it, would be considered a bad habit in that circumstance but there are other things, for example, that we warn people who have narrow blood vessels not to do. For example, weightlifting, which is an isometric exercise, or nearly isometric exercise, is very stressful to the system and increases the propensity to narrow blood vessels. It doesn't create disease. Weightlifting doesn't that we know of but it can take somebody who is getting along and turn them into somebody who is not getting along so well anymore, so that's a functional effect. And then if you tell them don't weight lift anymore, that impact is removed. And we think that people that are exposed to certain drugs have that happen to them, periodically come across that in practice, certainly people that take certain recreational agents, if you will, such as cocaine, for example, have that happen to them. That's one of the major causes of death associated with cocaine. It doesn't create heart disease but it takes a situation and plays havoc with it.

I assume, based on the science we have available, that the chemicals in cigarette smoke can also do that. And so if I tell people don't smoke,

then maybe that functional component will be alleviated.

Q. If you alleviate that functional component, don't you decrease morbidity and mortality for that individual as well, again related to coronary heart disease?

A. In a large population. I mean the reason we do this is the teaching is based on the epidemiologic studies in that large population. If a patient came to me and said can you give me a Midas-Muffler guarantee, if I stop smoking I'm not going to have a heart attack in six months, I can't do that. If 500 people came and I made that same -- did that same thing in terms of having them stop smoking or not take cocaine or whatever it is, the bad habit that we are talking about, then I could be assured that I would have a beneficial net effect on that population. So the short answer is: Functional things have to be looked at differently from things that cause disease.

MR. BORMAN: Can we take a short break now?

MS. FLYNN PETERSON: Sure.

(Recess taken from 2:38 to 2:50 p.m.)

BY MS. FLYNN PETERSON:

Q. Doctor, I'd like to refer you to that portion of your report where you talk about Minnesota Medicaid, the recipient population.

A. Just for speed --

Q. Page 8.

A. Okay.

Q. That portion of your report deals with the subject we touched just briefly on earlier today, and that is the influence of socioeconomic factors on the development of cardiovascular disease, and you have cited a number of references, I believe probably the last half dozen or so of your references dealt with that subject matter as well.

Is it your opinion that socioeconomic status in and of itself is a risk factor for the development of cardiovascular disease?

A. I would probably say that the standard risk factors for cardiovascular disease are the ones that we have identified of the 240 or whatever we talked about earlier, but that those risk factors might cluster in certain communities.

Q. What do you mean by that?

A. That there might be a higher penetration of risk factors in certain communities than others and there has been evidence provided in the literature to

suggest that lower socioeconomic class or lower economic class might, by virtue of a variety of reasons including, you know, what kinds of foods you can buy and other issues, lead to a greater penetration of certain adverse or certain undesirable risk factors. I think the only reasonable way to address that issue in terms of ascertaining the validity of it with respect to this population would be to open the books and look at who is at risk here and evaluate that population versus a control population. That apparently is not being permitted; consequently, one can only make inferences based on literature.

Q. And what do you mean, "open the books"?

A. Well if the population that's presumed to be the population of interest to the insurer is the Medicaid population in part, then the risk the insurer is taking with respect to the risk factor that we are arguing about or discussing would, under other circumstances, require us to look at the specific case and say, you know, this appears or does not appear to be relevant to this particular individual. So if we were discussing a single individual rather than a population, we would go through the medical record in detail and make some discussion about the

impact of whatever risk factor we were interested on that individual's health-care status. In a population, the same rule should apply inasmuch as that's not being permitted, at least that's my understanding.

Q. By "permitted" you mean you would have to look at every single Medicaid recipient?

A. In order to make a judgment as to the impact of the complaint and that patient's health care. In other words, you are taking rather large judgments with respect to statistical modeling of what the impact of smoking might be on a population, I think that's the essence of what's going on here, and those kinds of inferences are inevitably going to be arguable because they come down to looking at populations that we were not permitted to study. If one were permitted to look at the medical records of each of these people, one could perhaps come up with some assignment as to how much one thing or another participated in their -- in their health care.

I'm not trying to make work for myself, incidentally, since it would be an enormous project, but it would be an honest approach to developing a database that would be meaningful in regard to assigning risk of this, that or the other thing, or

not risk but impact of this, that or the other thing on the health care of the individuals in that population.

In the absence of doing that, in a statistically viable sample, or the whole population, we have to make inferences based on publications such as we have cited here. So if one wanted to beat on this paragraph to the extent that it isn't based on the specific population, then it's because I understand the population can't be examined in detail.

Q. But is that population really any different than the populations in many of these studies that you have cited?

Let me ask my question like this: In the population in the studies, for instance in the different studies that have looked at the incidence in epidemiological data from -- about coronary artery disease or coronary vascular disease, you are always looking at a group of people who have a variety of risk factors; isn't that true?

A. I think as a rule that's been the case.

Q. And in those studies there have been identified, for instance as you cited before, some 200 risk factors in one of the studies; correct?

A. Yes.

Q. And of those risk factors, various studies have quantified risk factors one way or the other but have determined the, quote, major, end of quote, and I understand you have -- you differ with respect to that term, you disagree with that, but we have seen a number of studies that have concluded there are some major risk factors.

A. Yes, we have.

Q. And so those populations have a variety of risk factors, but ultimately through a study of those populations some scientists and physicians have been able to conclude that there are major risk factors.

A. They have, that's right.

Q. Is this Minnesota Medicaid population any different from that? Just because there is a variety of risk factors and you haven't studied every individual, can't you still make some conclusions with respect to risk factors that affect that population?

A. Well I don't mean to be flippant. You can make conclusions if you are not concerned about whether you're right or wrong. The fact of the matter is, if you go and take Framingham data, and I suspect you have visited Framingham, Massachusetts, and if you haven't it's a very nice place to go, Framingham,

Massachusetts doesn't look at all like the central core of Minneapolis and yet Framingham is the -- I mean several of the classic studies that you've discussed here today with me are based on Framingham data and that's our gold standard virtually for the epidemiology of cardiovascular studies, all the quotations from Kannel and others, and so I think it's not just nitpicking to say that there could be substantial differences between Framingham, Massachusetts data and Minnesota Care data, especially given the fact there is other literature out there which suggests that socioeconomic factors play a role in tilting the table, if you will, in terms of risk factors.

So where your population of interest lies between one extreme and the other I don't know and I think it's not -- would not be unreasonable for us to try to learn about that because it could have very important implications. But to just accept that Framingham data is the same as central Minneapolis data is not reasonable.

And I'll go one step further just to give you a why I believe that to be the case. It's not just because Framingham, Massachusetts is a lovely village outside of Boston. It's because the nature of a

population that's willing, over 26 years, to go to a clinic every second year and have their blood pressure checked, their ECG checked, just to show up, is not a population that's at all comparable to populations of patients that we take care of where we can't get them to come to the clinic, I mean, when they are sick.

And so I think that there are good reasons to believe that there are differences in attitudes that have an impact on the patients, the individual's well-being. And so I think there is rationale for examining those two populations with a hypothesis they might be different in many respects.

Q. If cigarette smoking has been determined by the Framingham study to be a risk factor in the development of coronary heart disease, you would agree with that, wouldn't you?

A. Yes.

Q. Is there any reason to believe that with the Minnesota Medicaid population that cigarette smoking would not be a risk factor for that population of the development of coronary heart disease?

A. I think it's still likely to be a risk factor. The magnitude of the impact is what I'm getting at and the confounding variables that are going to be in

that population might be different, and that might be -- might provide a stronger argument for or a weaker argument. I wouldn't venture to guess up front. I would be surprised if the risk factor, that 1.68 or 1.7 we discussed turned out to be the same. That would surprise me. It might be higher or it might be lower. And I think the only way, if one is going to say that a certain risk factor has a certain impact on the health of the -- of a group of individuals is no; otherwise, how does one make these measurements.

Q. Dr. Benditt, you have cited reference 31, which is an article from the journal Circulation which we did discuss earlier this morning, is a publication of the American Heart Association.

A. Yes, item 31.

Q. That journal finds -- That journal discusses what we are talking about, socioeconomic factors and cardiovascular disease, and although it's not a study, what it is is a review of the literature; correct? Do you recall that?

A. That's correct. It is a -- I think it's another sort of review that examines data up to the early 1990s.

Q. Do you recall that that article found that the promotion of products associated with increased risk

of cardiovascular disease, tobacco and high-fat foods seem to be targeted toward lower socioeconomic groups?

A. I recall seeing something like that but I would appreciate it if I could take a quick glance at it.

Q. Does that article make the statement that I've just read to you, that the promotion of products associated with increased risk of cardiovascular disease, and the examples they give are tobacco and high-fat food, seem to be targeted toward the lower socioeconomic groups?

A. It does make that statement. What I'm trying to find is the basis that it uses for making that statement, and I think that whereas I don't have any intrinsic problem with that statement, it would be intriguing to me to know upon what research materials they make that judgment.

Q. Is socioeconomic status an independent risk factor for the development of cardiovascular disease, in your opinion?

A. No. I think it's dependent upon the other standard or well-accepted risk factors that we have discussed earlier but perhaps a greater penetration of certain of those risk factors.

Q. In your opinion, on the last page, page 9 of the

opinion, you note that "Minnesota Medicaid population is often is less likely to be compliant with treatment recommendations." What do you base that on, sir?

A. We didn't cite anything here. I think that basically what we are looking at is a -- is two things: One is just my personal experience and, two, the literature that deals with general populations. It's always difficult to make generalizations like this without seemingly oversimplifying matters and I think that we could probably have, if we had access to more information, done some detailed record search to try to prove that, versus a control population, something that really ought to be done.

Q. And did you attempt to review the medical records of those individuals who have been -- whose records have been part of this litigation?

A. Not to this point in time.

Q. Would that be helpful to you in drawing the conclusions you have reached in your report?

A. In drawing certain of the conclusions, it would be helpful, such as identifying how many other risk factors were prevalent in that population. There are certain risks, if you will, for doing that study, as you propose. One is that I don't have any assurance

that the population that's been defined is a statistically valid sample of the overall population, and, two, I would need to have a control population, comparable age-matched controls in whom we could make certain other judgements, such as again the prevalence of risk factors as well as the compliance for medical care. All of these are difficult things to measure.

Q. I'm trying not to repeat things we have already done, so I apologize as I'm looking through this material.

A. I appreciate that.

Q. We have skipped around a bit here.

Do you agree that cigarette smokers have higher rates of disability than nonsmokers, whether you measure by days lost from work or days spent in bed?

A. I don't have any personal knowledge on that subject.

Q. Have you been provided with any information with respect to what the damage model is in this case?

A. Not in a specific fashion. I am only aware that there is a -- one or two models that have been proposed that I assume is based on some sort of statistical assessment of the situation, but I'm not intimately familiar with them.

Q. Do you know --

What is your understanding generally?

A. Basically as I stated, that this is a model based on some inferences related to the role or the impact of smoking as a risk factor on health-care economics in a given population.

Q. Do you believe that smoking has any impact on the health-care economics of the Minnesota Medicaid population?

A. I'm sure it does.

Q. And why is that?

A. Well smoking is a risk factor for manifestations of cardiovascular disease and as such, since cardiovascular disease is a prominent health-care cost, manifestations of that disease cost money. The impact of that cost is something that health-care insurers are generally aware of, and a reasonable insurer would have to have considered the impact of various risks in their assignment of premiums related to health care. And inasmuch as we all in this room probably pay those every month, we are probably well aware of their impact.

Q. Dr. Benditt, one of the things you have stated in your report is the toxicological data from laboratory experiments are needed to bridge the gap

between the epidemiological evidence and the conclusion about causation. Do you recall that portion of your report?

A. Yes, I believe we made a statement of that nature.

Q. What types of animal studies would you propose would show or bridge that gap that the decades of human experience have not already shown?

A. Well decades of human experience haven't shown any of that. All they have really accomplished -- I shouldn't, again, diminish that accomplishment. These are important accomplishments. But what they have accomplished is weeding out for us important items, risk factors, if you will, for us to pursue further down the stream in terms of scientific study, and as I say, once again, I don't mean to demean those accomplishments. They are very important.

The kinds of studies is a much more difficult question because if it were intuitively obvious which ones to do, they would have been done by now. Nevertheless, I think we need to develop models that demonstrate or that can be used to try to demonstrate the impact of various disease processes on athero -- on the development of atheroma. A for example would be the concept of even cholesterol. High-cholesterol

diets in animals have been reported in some experiments of animals to show development of atheroma. I'm no expert in this area so I would defer to others, certainly. But my understanding at least is that -- that whereas there are -- there is evidence going in that direction, it's not incontrovertible yet, but at least there is progress made in that area. And understanding the development of atheromatous plaques, there is no reason why similar types of experiments couldn't be undertaken using other risk factors. In fact, I believe we do have certain experiments dealing with, say, hypertensive rats, specific type of rat that develops hypertension, that looks at the development of cardiovascular disease in a very short time frame.

So in certain aspects of risk factors, there has been progress in that regard. Whether we can say it's incontrovertible or not we would have to sit down with that literature and examine it, but at least there are examples where animal modeling appears to be going in the direction necessary to try to tie those -- the epidemiologic data to a scientific basis and there is no reason we couldn't look at it just for smoking. Inhalation studies may have been somewhat nebulous but the specific chemical

constituents of inhaled smoke or other presumed toxins.

Q. As I understand your testimony today, if those animal studies were to be conducted as you have discussed, they would explain the mechanism if they were successful; correct?

A. The -- The objective of the studies would be to try to ascertain the mechanism, but more importantly I think would be to try and identify the specific causative agents. I mean if, for example, we are dealing with tobacco smoke, and we made the statement earlier that there is umpteen different chemicals in there, can we identify one or two or three or thirty that are the necessary ingredients, or maybe there is not, you know, I think we have to go in open minded and see what we find, designing the experiments to identify each one or to examine each one in combinations.

There is reasonable likelihood that this could be done because we have precedence in hypertension and cholesterol experiments. The fact that it's not easy -- if it were easy I think we wouldn't be sitting here discussing this -- the literature would be available. The fact it isn't easy suggests this is a complicated problem and that very bright people

have been working on it for 15, 20 years, maybe longer, and we still have issues on the table.

Q. If those studies were to be conducted, do you believe that they would refute the associations that have been determined to exist between cigarette smoking and the development of coronary artery disease?

A. I don't think they would necessarily refute the associations but they might allow us to quantitate the relationships more precisely, and from my perspective, which is -- that would be the economic element. But from my perspective, it would allows us to perhaps design safer habits for people, if you will, and perhaps treatment strategies that could be of assistance in diminishing the adverse impact of risk factors.

Q. But you believe we would still see those associations between the risk factors of cigarette smoking and coronary heart disease?

A. We would see the associations. I think what you really want is can we develop a causal relationship that's scientifically valid. And it may be that there is one or it may be that you need several risk factors acting together at a cellular level to -- to get an effect, an adverse effect.

Q. Many of the studies that you have cited in your own references, however, have, in looking at the risk factors, controlled for risk factors and still determined that cigarette smoking is an independent risk factor; isn't that true?

A. Well they have controlled for the obvious large ones. I knew you were going to come to that. In other words, what you are saying is these are independent risk factors so how can they be related to other risk factors, but in actual fact what they have controlled for are the other major risk factors, so we know coronary -- that smoking is independent from hypertension and is independent perhaps from cholesterol, but is it independent of the other 243? We don't know that. Are there other factors, then, that play a role in facilitating the impact of smoking? We don't know. I mean, a for example is it appears that smoking is a more powerful risk factor in younger than older people. Why should that be? Well I suppose you could say that there are age-related differences that have an impact on whether a risk factor is important in a given population, and then we could start unwrapping the onion skin around that one, too, in going into, you know, what might those be.

Q. Haven't many of the studies concluded the reason for that is the older people have ceased smoking?
A. Well I'm not sure that I would agree with that. I think in the -- the -- a cynic might say those people who are susceptible to the obvious effect of the risk factor have already died and the people that are left over are immune. I'm not sure that -- I don't, frankly, believe that one either, but I think there are a number of relatively simple ways to try to argue why that observation might be, but, frankly, I don't think we know the answer today.
Q. Is it now your testimony cigarette smoking is not an independent risk factor in the development of coronary heart disease?
A. No. It's an independent risk factor to the extent that epidemiologic studies are able to examine risk factors, but there are no epidemiologic studies that examine the whole host of risk factors. They examine the principal ones that are controllable for, cholesterol, age, gender, hypertension.
Q. And that is a generally accepted methodology, and that is to look at the major causative agents when you are looking at a disease and not every possible cause; isn't that true?
A. Well yeah, it's acceptable but is it

scientifically dotting all the I's and crossing all the T's? I think not.

Q. In medicine, does every medical study dot all the I's and cross all the T's before making its conclusions?

A. Usually not, but most medical studies don't try to attribute risk of specific elements in a numerical fashion so I think that you are dealing with a very special case here, and when you deal with a special case you have to treat it a special way.

Q. One of the subject areas that we have discussed and you dealt with in your report is peripheral vascular disease.

A. Yes.

Q. We have looked at those components in the surgeon general's report which identify cigarette smoking as the most important risk factor in the development of peripheral vascular disease. Do you agree with that?

A. I believe that's what the surgeon general said.

Q. And do you agree with that?

A. No. I think the most important factor in the development of peripheral vascular disease is genetic predisposition.

Q. What role do you believe cigarette smoking plays

in the development of peripheral vascular disease?
A. It appears to be an important risk factor, and it may be the most important modifiable risk factor.
Q. You noted in your report that not all smokers developed peripheral vascular disease. That doesn't mean that it is not an important risk factor, does it, Dr. Benditt?
A. No, it doesn't. It just means that if there is a causal relationship between smoking and peripheral vascular disease, then we have to explain why it is that its penetrance is variable, and that may relate to the fact that diet, genetic predisposition and other factors that influence whether a patient will be susceptible to the sort of -- the additional risk factor attributed to smoking, or other risk factors for that matter, so again scientific investigation is needed. We shouldn't forget diabetes as a very important risk factor for peripheral vascular disease, too.
Q. Do you know whether in the damage model in this case, whether the data is drawn from the Medicaid population solely of Minnesota?
A. I can't speak to the damage model. I'd be happy to review it if you would like and comment, but I don't have enough specifics regarding it.

Q. Do you know whether there has been an adjustment for low income?
A. I'll have to make the same answer to that question. I have not been given insight into structure of the damage model and I might not even be qualified -- probably I'm not qualified -- to analyze it in a statistical fashion.
Q. One of the statements you made about compliance was with respect to the Medicaid population.
A. Yes.
Q. Let me review that again. What support do you have for that compliance other than your own practice? Is that the only basis that you are drawing that conclusion from?
A. That's principally based on my own observations, supported in part by the more general literature on socioeconomic factors and health care, some of which is cited also there.
Q. Do you know what percentage of your patient population are Medicaid recipients?
A. I would guess maybe about 20 percent.
Q. Okay. Are you familiar with the Mr. Fit studies?
A. Yes. It's been a long time since I've looked at publications related to Mr. Fit. I'm aware of the

studies.

Q. Do you know whether those were intervention -- interventional trials?

A. Those were behavior-modification trials, I was under the impression, including exercise, I guess is an intervention.

Q. How would you define an interventional trial or intervention trial?

A. Well I think any time you make a change in a habit or modify a behavior or provide a medication or do a procedure you have intervened, so any of those could be defined as an interventional trial. If you do multiple interventions simultaneously, then you obviously water down the impact of your understanding of what a specific intervention might have accomplished in that population.

Q. What role did the University of Minnesota play in the Mr. Fit trials?

A. The Public Health School was involved in the Mr. Fit trial and I wasn't a part of that.

Q. Were any of your patients a party to that, do you know?

A. Some of them were, yes, but most of the Mr. Fit trials start -- trials started prior to my coming to Minnesota in the late '70s.

Q. Do you know how many men participated and were screened in the Mr. Fit trial?
A. There were lots.
Q. Three hundred sixty-one thousand, six hundred sixty-two, is that consistent with your recollection?
A. Hundreds of thousands.
Q. And did this study establish cigarette smoking as an important risk factor for all causes of coronary heart disease and stroke?
A. I believe that was one of the outcomes. I would have to review the study outcomes in detail to confirm that.
Q. I believe that's one of the reports of that study. Just looking at the conclusion, is that one of conclusions that the authors state?
A. Yes, the authors indicate this is consistent with previous reports.
Q. In your opinion, was that a valid study?
A. This was a very helpful epidemiologic study. Again just -- not to detract from its importance but to just highlight the nature of the population, you are again talking about a highly motivated population who was willing to come for this kind of assessment, an intervention, and so whenever you read into the results of this you have to bear in mind this may not

be representative of a broad population of all types.

Q. In the discussion regarding the results of the study, do the authors indicate that the Mr. Fit results demonstrate the results of cancer and coronary heart disease mortality is substantially increased among smokers compared with nonsmokers and this risk increases with the number of cigarettes smoked?

A. They definitely state that.

Q. And in their conclusions do the authors state, in summary, the results of the Mr. Fit are consistent with other studies in demonstrating that compared with men who continued to smoke, men who stopped smoking have substantially lowered risk of both coronary heart disease and total mortality?

A. Yes, they make that statement. It should be pointed out that this is not a primary prevention study and in terms of addressing your question earlier of an intervention study, we can reasonably assume that a proportion, perhaps a large proportion of the population already had coronary artery disease and that the intervention would be cessation of smoking. The benefit is the benefit due to the functional improvements that we were discussing

earlier or a regression of the atheromatous disease, and I don't think that's addressed.

Q. Are you familiar with the study reported in the New England Journal of Medicine in 1985, Dr. Rosenberg and that research group regarding the risk of myocardial infarction after quitting cigarette smoking?

A. Yes, but it's been a long time since I've looked at this paper.

Q. Did that study include cigarette smoking as a major cause of myocardial infarction?

A. That's the opening line of the -- of the paper and they reference it, if I may, reference 1 of their paper, so that's -- I'm not sure that's the conclusion of their paper but they reference another paper which is an epidemiologic study, so I think that -- that we have to distinguish between the, if you will, opening gambit of their paper. Authors are always trying to get your attention and this one certainly does, but reference 1 I don't think provides the equivocal support for that statement that one would be looking for. If it did, then the 1983 surgeon general would have cited that paper, too.

Q. This is a 1985 study, however.

A. But the citation reference 1 is dated 1978.
Q. That's the Pooling project?
A. Yes.
Q. We will get to that in just a second.
With respect to the --
Do you disagree that cigarette smoking is a major cause of myocardial infarction?
A. I think the term "cause" again is an issue. I think the cigarette smoking is definitely associated with a higher frequency of myocardial infarction. The causes are probably multifactorial related to atheromatous disease, the functional aspects of smoking, including perhaps the impact of carbon monoxide in reducing oxygen transport, so I guess what I'm trying to say is the relationship is strong but the causal component, at least from a medical/scientific perspective I think is overstated in sentence one of that paper. I did not think that the authors of that paper actually came to such a strong conclusion themselves, and we could perhaps look at the conclusion of their own.
Q. That's my next question. With respect to their conclusion, did their results suggest the risk of myocardial infarction in cigarette smokers decreased within a few years of quitting to a level similar to

that of men who had never smoked?

A. And that's precisely what I was getting at. They are much more cautious in their conclusion than the opening gambit of their sentence -- of the paper.

Q. Isn't that the entire effect of this particular study, to assess the effect of quitting cigarette smoking?

A. It was, but the opening sentence that you pointed out says that there is a causal relationship and their paper does not speak at all to cause. It speaks again of important risk associations and --

Q. Dr. Benditt, is it a generally accepted view among cardiologists that cigarette smoking is a major cause of myocardial infarction?

A. I can't speak for most cardiologists. I think most cardiologists will paint that picture for their patients as part of the education and behavior modification we try to achieve, and we know that because there is this association with increased frequency of myocardial infarction in patients who smoke that that's probably good teaching to do for patients.

From a scientific perspective, what is the cause here is really beyond our resolution of knowledge and if you -- when I deal with a patient, I'm not dealing

with a discussion about scientific, you know, certainties. I'm trying to give just the benefit of a -- of what we think the knowledge to be. But if you ask me is this scientifically proven? The answer is: Not to my understanding.

Q. Are you familiar with the phrase "reasonable medical probability"?

A. I've heard that phrase.

Q. What does that mean to you?

A. Is there a likelihood based on current knowledge that there is a -- that X and Y are related or X caused Y.

Q. Do you believe to a reasonable medical probability that cigarette smoking causes myocardial infarction?

A. Yes, I think that my expectation is that there is a cause relationship there but it may not be through anything related to the development of atherosclerotic disease. It may be through functional aspects that we talked about earlier. And that's a personal opinion not based on any specific scientific evidence and so I'm very cautious about providing those in an environment where you want, you know, hard data. In a patient conference where I'm dealing with patients, I think physicians, including

myself, would be more likely to try to change behavior based on that kind of argument rather than scientific means.

Q. Physicians don't wait for scientific proof to the degree you described it before trying to help patients prevent disease, do they?

A. As a general rule, no. And often times that's beneficial. But there have been many instances in which that's proved to be harmful, so there is two sides to that coin.

Q. What instances come to mind?

A. Well the classic example in medicine is the use of cryothermia for the treatment of stomach ulcers, a very popular form of therapy with a lot of intuitive common sense to it that proved to be a catastrophe. That's number one. Number two, the opposite side of the coin is that in the early 1970s it was generally considered bad medicine to anti-coagulate patients who had strokes, and intuitively that makes sense. Now it's considered to be good medicine to do that most of the time. So the science often follows years behind practice and I think people make practice judgments based upon good intentions but that periodically the knowledge base shows that we were wrong.

Q. The surgeon general first identified cigarette smoking as a potential risk factor in coronary heart disease in 1964; correct?

A. That's my understanding.

Q. And in the 30-plus years since then, has there been any evidence that the surgeon general is wrong in that conclusion?

A. In terms of the risk-factor judgment, I don't think so.

Q. I'd like to talk to you now about the Framingham studies that we have discussed earlier today, so I'm just going to get those. How we doing on time?

What was the study, Dr. Benditt?

A. Framingham study was a cohort study in a small -- in a small town, not a small population, outside of Boston, Massachusetts that consisted of the biannual examination of a volunteer population over a 26-year period, so they had 13 biannual examinations, primarily dealing with public-health concerns such as the effects of blood pressure, cholesterol, stroke, age and other general types of medical information and try to correlate that to disease processes in that population.

Q. And did that study encompass over 4,000 subjects?

A. I can't remember the number but that probably is right, yes.
Q. Do you know whether that study concluded there was an increased risk of myocardial infarction or death associated with cigarette smoking in all combinations of high, low systolic blood pressure and cholesterol levels?
A. Yes. I'd like to see what you are quoting from, but I think it's consistent with my understanding of the outcomes of this study of which there is multiple publications, as you are aware, and I think it was this study that identified that with respect to the other well-known risk factors, that this was an independent risk factor.
Q. Did this study also look at cigarette smoking as a risk factor for stroke?
A. Yes.
Q. And did it conclude that cigarette smoking was a significant independent contribution to the risk of stroke generally and brain infarctions specifically?
A. I believe that's correct. Again I'd like to take a look at that paper to confirm the statement, but I believe that's true.
Q. Where I started reading was: "This cigarette smoking continued to make a significant..."

A. Yes.
Q. Does the Framingham study with respect to stroke that we are discussing, does it also reference other epidemiologic studies that also came to the same conclusion relative to the relationship between smoking and stroke?
A. Yes, it references other epidemiologic studies. Of curious note, they reference studies using death certificates, which are notoriously unreliable. I think we have better epidemiologic studies than that.
Q. It talks about studies in Finland, talks about a study, the Honolulu Heart Project, and does it then conclude that these -- confirming that in the Framingham study findings, cigarette smoking was found to exert a significant independent impact on stroke incidence after taking other stroke risk factors into account and even after excluding subjects with coronary heart disease?
A. Yes, that's their statement.
Q. And then you can see here where the report talks about the Framingham study and its own data. After it talks about these studies would have been discussed in Finland and Honolulu does it then conclude that these data show risk factors --

(Interruption by the reporter.)

-- does it then conclude that these data show cigarette smoking to be a risk factor for smoke in both normal tensive and hypertensive subjects and in women as well as men? In fact, even after other cardiovascular risk factors were taken into account, cigarette smoking continued to exert significant independent impact on stroke incidence?

A. Yes, it reaches that conclusion.

Q. Does this study further state that the causal connection between smoking and stroke, like that between smoking and coronary heart disease, is supported by all the traditional epidemiologic proofs?

A. It makes that statement, and we could debate the meaning of that statement. I think traditional epidemiologic proofs are a debatable way to make a causal relationship. That is no doubt what you read, is what they said.

Q. Further, do the authors of this study say on the basis of these data stroke can assuredly be added to the list of disabling and lethal diseases permitted by cigarette smoking?

A. That's correct, I think that's -- that's what they said.

Q. What was the Pooling Project?
A. Well I would have to go back into it myself since it was a long time ago, and I can't say that I've ever read that tome in great detail but it's a epidemiologic study that dates back to the mid 1970s.
Q. Doctor, this is an article from the Journal of Chronic Diseases. Let's see if I can get you a better cite there. It was a lot easier to read these studies?
A. As I got older, it's more difficult.
Q. And then to read them upside down.
It's from the Journal of Chronic Diseases, 1981, and does this appear to be the Pooling Project research group, a report regarding that group?
A. Yes.
Q. And in the title of the article it talks about the relationship of blood pressure, serum cholesterol and smoking habits, relative weight and ECG abnormalities to the incidence of major coronary events, and it says, "FINAL REPORT OF THE POOLING PROJECT"?
A. Yes. And basically what they did is they -- it's not an independent study.
Q. Uh-huh.
A. It was basically what its name implied. They

pooled data from about five other major epidemiologic studies including the Tecumseh project and the Alabama project and the Framingham data and a couple others.

Q. Is this a respected study?

A. I think the reference is respected, I think the individual studies themselves are, especially the Albany study, and the Framingham study and the Tecumseh study, too, are more -- are better prime resources of data, but I don't have any qualms about reviewing the combination there.

Q. Referring you to page 261 of that article, does it state that the cigarette habit is confirmed as a pernicious, powerful risk factor?

A. I must admit, you will have to pardon the expression, that we could never get away with writing like that in the 1990s. I'm not sure exactly how to quantitate a pernicious powerful risk factor.

Q. Is that what this study and these --

A. That's what it says.

Q. -- concluded? Okay.

A. Yeah, I mean it's -- the medical literature has become a lot dryer in recent years.

Q. When the major risk factors --

Does the study go on to say when the major risk

factors, number one, blood pressure, number two, serum cholesterol, number three, cigarette use, are considered simultaneously by applying a multiple logistic model, it is further demonstrated that the -- it is demonstrated that consistently the relationship of each of these traits to coronary artery --

A. Proneness.

Q. -- proneness is an independent one?

A. Yes, that's what it says. That's consistent with what we have discussed earlier.

(Discussion off the record.)

Q. Do you know how many compounds in tobacco smoke are known to be carcinogenic?

A. It's outside of my area of expertise. I can't answer that.

Q. Do you know how many compounds in tobacco smoke are toxic?

A. No, I don't. I guess it would depend on toxic to what.

Q. How would you define "toxic"?

A. Well I'm not quite sure I can define toxic. I think it's in this sense a -- meant to be a very qualitative statement because even things that are beneficial could be toxic in undesirable

concentrations, so I can't give you a meaningful definition in this context.

Q. Do you have an opinion as to whether or not secondhand smoke is a cause of coronary heart disease?

A. My opinion would be that secondhand smoke is associated with and a risk factor for coronary artery disease.

Q. In your opinion, how strong is that association?

A. The strength of an association, I guess, is something that we have been discussing a lot today and if we said that -- and all I could do would be to give you a guess, because I don't recall offhand a direct number, so if a guess is permitted it would probably be a risk factor probably somewhere in the range of 1.2 to 1.3.

Q. Have you ever been provided with any tobacco company documents, internal documents that indicate that cigarette smoking is related to coronary heart disease?

A. No.

Q. Do you know whether the cigarette industry has ever undertaken any studies to determine whether there is any relationship between tobacco smoking or tobacco use and coronary heart disease?

A. I'm not aware of any.
Q. When you met with attorneys to discuss your opinions in this matter, did you yourself make any notes?
A. The only notes I made is where this room was, where we were meeting today.
Q. So when you had the meetings before your -- the first draft of your report was generated, did you yourself make any notes?
A. No.
Q. When you were reviewing the research and articles, have you made any notes for yourself?
A. Only mental.
Q. Are you in the practice of highlighting or making margin notes on articles when you review them?
A. No, I'm not.
Q. Have you worked as an expert witness before this case?
A. Yes, I have.
Q. And on how many occasions?
A. I think we submitted information on as many cases as I could recollect, but probably three or four. Two of them relate to patent litigation and three to product liability, roughly may be plus or minus one.

Q. Have you ever testified in -- by way of deposition before?
A. Yes, I have.
Q. And was that in connection with being an expert witness?
A. Yes, that's correct. I have also done depositions related to certain medical malpractice situations where I was an expert witness. I think we provided some information regarding that.
Q. And have you ever testified in a courtroom before?
A. Yes, I have.
Q. On how many occasions?
A. Probably four or five.
Q. And in what types of circumstances?
A. One was a -- related to the nature of a sudden episode that an insurance company was concerned about, one was in defense of a malpractice claim against the Mayo Clinic, two were related to patent infringement cases and one -- two, actually, now that I think about it, were related to product liability issues.
Q. Are you currently involved in any research?
A. Yes.
Q. What type of research are you involved in?

A. Essentially two types: One relates to the assessment of patients with fainting spells that relate to heart-rhythm disturbances, and we are interested in the specific impact of the central nervous system that has the results of patients fainting or blacking out, and that's perhaps our most important clinical research, also has some experimental aspects, animal experimental aspects to it, and another relates to developments in cardiopulmonary resuscitation, experimental studies.

Q. Have you ever submitted proposals for research with respect to the issues we have been discussing here today in relation to cigarette smoking as a cause of coronary heart disease?

A. No, I have not.

Q. We had spoken earlier this morning about Dr. Graham's report and you had asked that I provide you with a copy since you had not had an opportunity to review it recently, so I have brought a copy of Dr. Graham's report and I would like to ask you some questions about that. Would you like an opportunity to review it first?

A. No, we can just go ahead, and if I have a problem, I'll slow down.

Q. Are there any -- Well one of my questions will

be a general one, whether you have any areas of disagreement with Dr. Graham in his report.

A. That would require me to read the report once again to assure myself that he didn't say something that I may have forgotten.

Q. Okay.

MS. FLYNN PETERSON: I probably have I would say about another hour, hour and a half to be done. Do you want to review this tonight and we can ask questions about that, or do you want to take ten minutes to review it and deal with this tonight?

THE WITNESS: My vote would be to forge ahead if that doesn't cause a problem for others.

MS. FLYNN PETERSON: And we will still conclude at four thirty.

THE WITNESS: Or we could go on later if you like. I -- I'm at your disposal until probably --

MR. BORMAN: I guess you're thinking -- We can go off the record.

(Discussion off the record.)

(Deposition concluded at approximately 4:00 o'clock p.m.)

C E R T I F I C A T E

I, David A. Campeau, hereby certify that I am qualified as a verbatim shorthand reporter; that I took in stenographic shorthand the foregoing deposition of DAVID G. BENDITT. M.D., at the time and place aforesaid; that the foregoing transcript, Volume I, consisting of pages 1 - 198, is a true and correct, full and complete transcription of said shorthand notes, to the best of my ability; that the noticing party has been charged for the original transcript, and that ordering parties have been charged the same rate for such copies of the transcript.

Dated at Lino Lakes, Minnesota, this 15th day of September, 1997.

_____

SIGNATURE PAGE

I, DAVID G. BENDITT. M.D., the deponent, hereby certify that I have read the foregoing transcript, Volume I, consisting of pages 1 - 198, and that said transcript is a true and correct, full and complete transcription of my deposition, except per the attached corrections, if any.

(Please check one.)

____ Yes, changes were made per the attached (no.) _____ pages.

____ No changes were made.

_____

DAVID G. BENDITT. M.D.

Sworn and subscribed to before me this day of , 199__.

_____

Notary Public

My Commission expires: (DAC)